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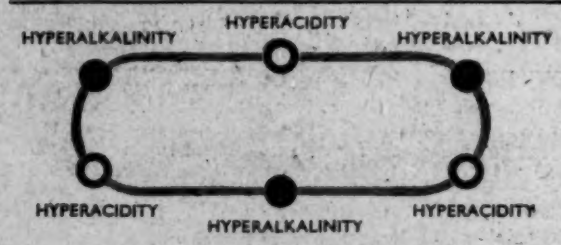

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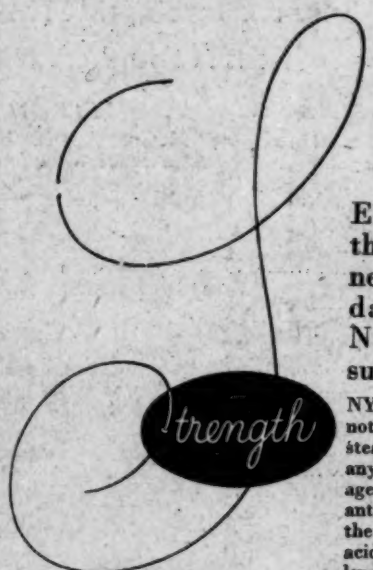

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BRITISH MEDICAL JOURNAL

LONDON SATURDAY MAY 1 1943

THE INVESTIGATION OF HAEMOLYTIC TRANSFUSION REACTIONS*

BY

P. L. MOLLISON, M.B., M.R.C.P.

A haemolytic transfusion reaction may be defined as the occurrence of an abnormal destruction of the red cells of either the donor or the recipient immediately after transfusion. Following a normal compatible transfusion of fresh blood the donor's erythrocytes are destroyed only at a slow rate, approximately 1% of the total being eliminated each day; since this is (presumably) the rate of destruction of the recipient's own erythrocytes no signs of increased blood destruction are observed. When incompatible blood or blood that has been stored for an excessive length of time is transfused, however, the donor's erythrocytes are rapidly destroyed and signs of increased red cell destruction develop. Destruction of some of the recipient's *own* red cells may follow the transfusion of blood the plasma of which contains high-titre incompatible agglutinins.

When transfusions are given to persons affected with certain varieties of haemolytic anaemia the signs of haemolysis may temporarily become more pronounced. Such reactions may not be due to one of the causes already considered, and may be listed as rare varieties of haemolytic transfusion reactions.

Haemolytic reactions may be mimicked by the injection of haemolysed blood. This, by the above definition, cannot be considered as a true haemolytic reaction, since the destruction of the donor's erythrocytes precedes transfusion. Nevertheless, the signs produced may be indistinguishable from those of true haemolytic reactions. These various types of haemolytic reaction may be indistinguishable clinically. Each may give rise to jaundice, with or without haemoglobinuria, and each, if fatal, may produce the same post-mortem appearances. On the other hand, each variety may pass unnoticed unless special tests are applied. The purpose of this report is to discuss the pathological features of each type and to describe methods of differential diagnosis.

The establishment of the diagnosis falls conveniently into two parts: (1) the demonstration of the occurrence of increased blood destruction; and (2) the demonstration of the cause of the increased destruction.

The Signs of Increased Blood Destruction

The signs produced by increased blood destruction vary according to whether destruction is predominantly intravascular or extravascular (intracellular).

Intravascular Destruction.—Intravascular destruction results in the liberation of haemoglobin into the plasma. Knowledge of the rate of removal of free haemoglobin from the blood stream has been chiefly derived from experiments in which haemoglobin solutions have been injected intravenously into human subjects. The rate of elimination varies with the initial concentration, being more rapid at high concentrations. For instance, when the initial plasma level is approximately 200 to 300 mg. per 100 c.cm. 50% or more may be removed in three hours (Ottenberg and Fox, 1938), although the plasma may not be entirely cleared for from 8 to 12 hours (Ottenberg and Fox, 1938; Gilligan *et al.*, 1941). When the initial plasma level is only 40 to 60 mg. per 100 c.cm. the plasma may not be cleared for 5 hours.

Haemoglobin liberated intravascularly may be dealt with in three different ways (Fairley, 1940). (1) It may be absorbed by the reticulo-endothelial system and converted to bilirubin, which is then discharged into the blood stream and excreted by the liver. This is probably the only mechanism brought into play when intravascular haemolysis is slight. (2) When intravascular haemolysis is of greater degree part of the haemoglobin is broken down intravascularly and haematin is liberated; this combines with serum albumin to form methaemalbumin, a pigment which may be recognized by spectroscopical examination or, when it is present in only small amounts, by Schumm's test (Fairley, 1940). The rapid intravenous injection of 14 g. or more of haemoglobin (equivalent to the rapid intravascular breakdown of 100 c.cm. of blood) will lead to the formation of sufficient methaemalbumin to produce a positive Schumm reaction, but the rapid intravascular breakdown of two to three times this amount is necessary to produce enough methaemalbumin to be recognized spectroscopically. Methaemalbumin may be detected in the plasma 5 hours after the intravenous injection of haemoglobin, and then persists for 24 hours or more (above data from Fairley, 1940). (3) Some haemoglobin is excreted by the kidney, but only when the concentration of haemoglobin in the plasma exceeds approximately 135 to 180 mg. per 100 c.cm. (Gilligan *et al.*). This concentration may be reached after the rapid intravascular breakdown of approximately 60 c.cm. of blood. Patients who are already passing albumin in the urine may excrete haemoglobin at a lower threshold (Gilligan *et al.*). Once haemoglobinuria has begun it may continue when the plasma haemoglobin level has fallen far below the initial threshold, so that haemoglobinuria may persist for 24 hours or more after transfusion.

When the urine is alkaline the majority of the haemoglobin will be present in the form of oxyhaemoglobin and the urine will be red in colour. If the urine is neutral or acid, however, methaemoglobin will be formed and the colour will be brown or black. Moreover, acid haematin will be precipitated in the kidney tubules, and small casts of this substance will be found in the urine. The latter may persist for several days after transfusion.

Haemoglobinuria is always accompanied by albuminuria (Gilligan *et al.*), and when haemoglobinuria follows an incompatible transfusion it may also be accompanied by glycosuria, as shown in animal experiments by Ottenberg and Thalhimer (1915) and as exemplified by Case 6 below.

Following intravascular haemolysis, some degree of renal failure may occur, with oliguria and a progressive increase in the blood urea concentration. This renal insufficiency is thought by some authorities to be due to blockage of the renal tubules with acid haematin, a relatively insoluble compound of haemoglobin which is formed in acid urine. This theory was originally based on the observations of Baker and Dodds (1925), who showed that in rabbits renal failure after the injection of haemoglobin solutions could be prevented by alkalinizing the urine. The theory has been challenged by De Navasquez (1940), who believes the anuria is the result of a decrease in the rate of blood flow through the glomeruli. DeGowin *et al.* (1938)

* A report to the Medical Research Council from the S.W. London Blood Supply Depot.

have stated their belief that, in man, blockage of the tubules is insufficient in many cases to account for the degree of renal failure, and they believe that damage to the tubules by some "nephrotoxic factor" may be responsible.

When renal damage occurs signs of uraemia may not be apparent until at least the second or third day after transfusion, and meanwhile the recipient may appear well. Thereafter a critical phase occurs, usually between the sixth and twelfth days (Bordley, 1931), in which the patient may become comatose and die or else start passing large quantities of urine and recover.

Extravascular Destruction.—The extravascular destruction of red cells results in the production of bilirubin. The degree of bilirubinaemia depends upon the rate of blood destruction and also upon the efficiency of the liver in removing bilirubin from the blood stream.

Signs Common to Blood Destruction, whatever the Mechanism

When, as the result of intravascular or extravascular destruction, the serum bilirubin concentration exceeds 4 mg. per 100 c.cm. (approximately) the recipient becomes jaundiced. Although the serum bilirubin concentration rises rapidly after red cell destruction, usually reaching a peak 5 to 6 hours later (Vaughan, 1942), clinical jaundice is unlikely to occur before the end of 12 hours or so, because time is required for staining of the tissues. As mentioned above, the degree of bilirubinaemia depends upon the rate of blood destruction, so that slow blood destruction is less likely to produce jaundice, other factors being equal. It may also be mentioned that the other main factor affecting the onset of jaundice—namely, the adequacy or otherwise of liver function—may be affected by the transfusion of incompatible blood. Following such a transfusion, evidence of liver damage is sometimes apparent at necropsy and may be manifested during life by the development of signs of toxic jaundice after transfusion. For instance, the van den Bergh reaction may become "direct" (see Case 5) and bile pigments may appear in the urine (see Case 6). Normally, once the destruction of the blood is complete the serum bilirubin concentration falls again, and has usually returned to the pre-transfusion level by the end of three days, and jaundice of the patient seldom lasts for more than two or three days after transfusion.

Because of the blood destruction, the increase in haemoglobin concentration expected as a result of transfusion does not occur when there is a haemolytic reaction. Evidence based on haemoglobin estimations before and after transfusion may be misleading, however, because the patient's haemoglobin concentration may be changing at the time of transfusion (due to the nature of the anaemia, for instance) or the patient's blood volume may undergo alteration. For this reason far more reliable evidence may be obtained in the majority of cases by estimating the survival of the transfused cells by the differential agglutination technique (see below).

Apart from the signs of increased blood destruction, the recipient may show signs of constitutional disturbance and complain of symptoms. For instance, a rise in temperature with or without a rigor is common and the transfusion of incompatible blood may be followed by particular symptoms, which are referred to below. It is important to realize, however, that a haemolytic transfusion reaction may occur without giving rise to any symptoms; and, conversely, it must be emphasized that in the majority of cases the occurrence of a rigor following transfusion does not indicate blood destruction.

Although it is possible to make a theoretical distinction between extravascular and intravascular destruction it is doubtful whether the distinction is a valid one. It may be that destruction is always intravascular, but that when it occurs slowly the free haemoglobin in the plasma never reaches a detectable concentration because it is rapidly absorbed by the reticulo-endothelial system, probably at the site of liberation. That this is so is suggested by the observation that in mild haemolytic anaemias no free haemoglobin can be detected in the plasma as a rule, although in an exacerbation haemoglobinaemia and haemoglobinuria may be noted. It is doubtful whether this represents a change in the mode of destruction, and it seems more likely that it merely indicates an increase in the rate of destruction.

In describing the signs characteristic of various types of haemolytic reactions it should be borne in mind, therefore, that when the signs of extravascular destruction occur the inference is probably simply that destruction has taken place at a slower rate than when the signs of intravascular destruction are noted. There are, however, other features of the various types of haemolytic reaction which are of some assistance in arriving at a correct diagnosis, and these different types will therefore be described.

Destruction of Incompatible Blood

Incompatible red cells may be either agglutinated or haemolysed by the recipient's plasma *in vitro*. Only about 30% of sera will haemolyse as well as agglutinate cells containing the corresponding agglutinogen (Wiener, 1939), but it is important to realize that even when only agglutination occurs *in vitro* intravascular haemolysis may occur *in vivo*. For instance, when Rh-positive blood is transfused to a recipient whose serum contains anti-Rh agglutinins severe intravascular haemolysis may follow (see Case 6, below, and cases described by Wiener and Peters, 1940), although haemolysis never occurs *in vitro* when Rh-positive cells are incubated with sera containing anti-Rh antibodies. The chief factors affecting the mode of destruction would appear to be the titre of the incompatible agglutinins in the recipient's plasma and the rate of transfusion.

In practice intravascular haemolysis is common after incompatible transfusions, although not invariable (see Case 5, for instance). When intravascular haemolysis occurs it is often followed by some degree of renal failure.

After the transfusion of incompatible blood, clumps of agglutinated donor cells may be found in blood samples withdrawn from the recipient. These agglutinates may persist for at least 48 hours after transfusion (as in Case 4), although they may not be detectable in a sample taken immediately after transfusion (as in Case 5). It may be added that whenever there are preformed agglutinins incompatible with the donor blood—that is to say, when the anti-A or anti-B agglutinins are involved or when atypical incompatible agglutinins (usually anti-Rh) are present in the recipient's plasma at the time of transfusion (as a result of previous stimulation by pregnancies or transfusions)—the majority of the donor cells are usually eliminated within a few hours of transfusion. In such cases the agglutinins in the recipient's serum undergo characteristic changes in titre (Rø, 1937; Wiener *et al.*, 1941; Mollison and Young, 1941). There is usually an initial reduction in titre, lasting for one to two days after transfusion, which is probably due to absorption by the incompatible erythrocytes. Then there is a rapid increase, which usually reaches its peak 10 to 20 days after transfusion. Observation of these changes may present valuable evidence, particularly when the donor cannot be traced. When the recipient's plasma does not actually contain incompatible agglutinins but there is potential incompatibility, as when Rh-positive blood is transfused to an Rh-negative recipient, the rate of elimination is variable. If the recipient fails to react to the stimulus of the foreign agglutinogen contained in the donor blood the latter may survive perfectly normally in the recipient. Even after a first transfusion, however, in a person not previously immunized, the recipient may respond by producing anti-Rh agglutinins (although slowly), so that the total survival of the donor cells is reduced from the normal 100 to 120 days to about 60 days (Dacie and Mollison, 1943). In such a case it is of course impossible to detect signs of increased pigment metabolism, and the only evidence of increased blood destruction is the diminished survival time of the transfused cells. In cases in which the recipient has been sensitized by previous transfusions of Rh-positive blood he may respond to a further transfusion by a rapid production of anti-Rh agglutinins and the rapid elimination of the donor cells (i.e., within five to seven days of transfusion). In such a case an increase in serum bilirubin may be detected and the response to transfusion from the point of view of increase in haemoglobin concentration is disappointing (see Wiener, 1941, and Case 1 described by Boorman, Dodd, and Mollison, 1942). Although any case in which the survival of the donor cells is diminished may be considered to be an instance of a haemolytic reaction, the term is in practice restricted to those cases in which destruction starts during transfusion. The term "inapparent haemolysis" has been applied by Wiener to cases in which destruction occurs more slowly after transfusion.

Immediately after the start of a transfusion of incompatible blood the patient may complain of severe lumbar pain (see Cases 1, 2, and 3, for instance), together with various other symptoms, such as burning of the face, tightness of the chest, etc.; some degree of collapse followed by a rigor is common. These symptoms may be delayed, however (see Cases 5 and 6), or abolished by morphine (see Case 3), or may be entirely absent (Case 4). Conversely, they may be produced by the transfusion of apparently compatible serum. One has the impression that the sequelae of the transfusion of incompatible blood are less severe now than formerly, and, if true, this may be due to the increasing tendency to administer blood at a drip rate (apart from cases of acute haemorrhage and "shock"), compared with the more rapid rate that used to be adopted.

Destruction of Stored Blood
(Data from Mollison and Young, 1942)

The rate of destruction of the erythrocytes of stored blood in the circulation of a normal recipient after transfusion depends mainly upon their previous length of storage, the preservative solution used, and the temperature of storage. The erythrocytes of blood stored with a citrate–glucose diluent (M.R.C. War Memorandum No. 1, 1940) at 5° C. for periods up to 10 days or so survive very well in the recipient's circulation, only a very small proportion being broken down during the 24 hours following transfusion and the total survival time being for all practical purposes indistinguishable from that of fresh blood. The increase in serum bilirubin concentration in the recipient's plasma after such a transfusion seldom exceeds 1 mg. per 100 c.cm. Even when the period of storage in this diluent reaches 21 days only about one-fifth of the erythrocytes are destroyed during the 24 hours after transfusion, and the increase in serum bilirubin concentration is unlikely to exceed 2 mg. per 100 c.cm. in our experience, although it should be noted that greater increases were found by Vaughan (1942). The transfusion of blood stored for 21 days in citrate–glucose mixtures is not followed by haemoglobinaemia, and, as Vaughan has shown, methaemalbuminaemia does not occur. Thus, following the transfusion of blood previously stored for 21 days or less with the preservative solution which is in general use, the only signs of increased blood destruction will be the small increase in serum bilirubin (only to be detected by the taking of a venous sample within a few hours after transfusion) and a slightly diminished survival of the donor cells; and the response should be scarcely less satisfactory even from the point of view of the increase in haemoglobin concentration than when fresh blood is used.

The erythrocytes of blood stored in a simple solution of sodium citrate, however, survive far less well in the recipient's circulation than the erythrocytes of blood stored for a similar period in a solution to which glucose has been added. For instance, the erythrocytes of blood stored for, say, 17 days in a simple sodium citrate solution are almost completely eliminated from the recipient's circulation within 24 hours of transfusion. A part of this destruction occurs instantaneously, owing to the rupture of the most fragile cells in the recipient's plasma, although the majority of the cells are not destroyed in this way. The haemoglobinaemia produced by this intravascular destruction is reinforced by the amount of free haemoglobin present in the plasma of the transfused blood, since blood stored with sodium citrate alone haemolyses far more rapidly than blood stored in solutions containing glucose (Rous and Turner, 1916). For instance, blood stored in sodium citrate is about one-tenth haemolysed by the end of 21 days, whereas blood stored for a similar period in citrate–glucose is only about 1% haemolysed. Thus the use of blood stored in a simple citrate solution for 17 days or more is very likely to produce haemoglobinuria and jaundice in the recipient. It may be mentioned that some of the prejudice that still exists against the use of stored blood dates from the early days of the present war, when glucose was not added to blood during storage.

Blood haemolyses more rapidly at room temperature than at 5° C., and it is almost certain that the power of the intact erythrocytes to survive in the recipient's circulation is adversely affected by prolonged exposure to room temperature. It is, however, only of academic interest to separate the effects of the injection of free haemoglobin from the effects of the more rapid destruction of the intact erythrocytes, and it is simply necessary to realize that blood that is left standing about at room temperature before transfusion may give rise to the signs of blood destruction when it is transfused. It may be added that blood stored in the standard 540-c.cm. bottle does not reach room temperature for approximately five hours after being removed from the refrigerator (Oliver and Young, 1940).

Destruction of Recipient's Red Cells by High-titre Incompatible Agglutinins

Intravascular agglutination and haemolysis, followed by bilirubinaemia, have been produced experimentally by the injection of plasma containing high-titre incompatible agglutinins, but only when these agglutinins were present in exceptionally high titre (Aubert *et al.*, 1942). When group O blood the plasma of which contains very-high-titre agglutinins is transfused to recipients of other groups, and a haemolytic reaction follows, it is of course possible to demonstrate that the donor cells survive normally and that it is the recipient's cells which are destroyed (Aubert *et al.*, unpublished observations).

Haemolytic Reactions in Persons Affected with Haemolytic Anaemias

The transfusion of blood to patients affected with at least one variety of haemolytic anaemia may result in an exacerbation of the haemolytic process for a cause other than one of those already mentioned. As an illustration, in a case of nocturnal haemoglobinuria observed by Dacie and Firth (1943) the transfusion of agglutinin-free plasma resulted in the production of haemoglobinaemia, and the transfusion of a concentrated suspension of red cells brought about a very violent haemolytic reaction which was not due to the destruction of the donor cells, since, in fact, the latter survived normally (Dacie and Mollison, 1943).

Haemolytic Reactions Simulated by the Transfusion of Haemolysed Blood

Blood may become haemolysed by the action of contaminating organisms, by being overheated, or by being stored for excessive periods under unsuitable conditions. Certain bacteria will grow freely in stored blood at refrigerator temperature. These organisms usually cause haemolysis of the blood, so that, apart from the possible toxic effects of the bacteria or their breakdown products, the transfusion of infected blood may be followed by the signs of a haemolytic reaction. The consequences of the transfusion of infected blood may be very serious (as in Case 11). When blood is carelessly heated before transfusion it may become haemolysed—for instance, if it reaches a temperature of approximately 55° C. and is kept at that temperature for more than 10 minutes. Inquiry should always be made, therefore, to find out the method of heating (if any).

As mentioned above, blood may become grossly haemolysed if left for a long time at room temperature. The results of the transfusion of blood that had become haemolysed in this way are illustrated by Case 10 (see below).

Investigation of Haemolytic Reactions

At the outset it may be mentioned that the investigation of transfusion reactions suspected of being haemolytic in nature is greatly facilitated if certain samples are available at the time of investigation. These are: (1) a sample of the donor blood, and (2) a pre-transfusion sample of the recipient's blood. In order that these samples shall be available when they are wanted it is desirable that they should be obtained as a routine and kept for a period of 24 hours after every transfusion. It may prove impracticable to obtain a pre-transfusion sample of blood from the recipient before every transfusion, but it should be made an invariable rule that a sample of the transfusion fluid is kept. This is most easily secured by leaving the dregs in the bottle. The apparatus used may be washed immediately after transfusion, but the bottle itself should be recapped and put on one side, preferably in the refrigerator. In all cases the name of the donor or the serial number of the bottle of transfusion fluid should be recorded on the patient's notes. When there is a detachable label on the bottle this should be fastened to the notes.

When pre-transfusion samples of blood are taken from the recipient as a routine they may be conveniently obtained

through the needle used for transfusion if the latter is connected with the apparatus by means of an adaptor. Ideally, a few cubic centimetres of blood should be taken into a plain tube and allowed to clot, and a similar quantity should be taken into a tube containing oxalate. These samples should be kept in a refrigerator and not be discarded until the end of 24 hours after transfusion, when the patient has been seen again and been found to respond favourably to the transfusion. When the patient is seen within 24 hours after a transfusion and a haemolytic reaction is suspected, a large sterile venous sample of blood should be obtained and also a clean sample of urine. If the patient is seen later the same samples should be obtained, although many of the tests set out below will be inapplicable.

Precautions to be Observed in Obtaining the Venous Sample.—A large (20 c.cm.) sterile syringe with a needle of not less than 20 S.W.G. should be used. The syringe and needle should be absolutely dry or else must be rinsed in sterile isotonic saline. Venepuncture must be clean. After venepuncture the needle must be removed from the syringe before the blood is squirted into the sample tubes. The sample should be partitioned between two plain tubes (one sterile) and one tube containing dry oxalate.

The Sample of Urine.—It will be sufficient to obtain a clean sample of urine, unless there is any risk of contamination with blood (in a recently delivered woman, for instance); in such cases a catheter sample must be obtained.

Examination of the Samples

In an obscure case the majority of the following tests may have to be made:

(*a*) *Donor's Blood (from the Transfusion Bottle if Possible).*—(i) A sample should first be withdrawn from the bottle with a sterile pipette and kept in a sterile tube in case bacteriological examination is required. (ii) A mixed sample should next be centrifuged to determine the amount of free haemoglobin in the supernatant plasma. (iii) The blood should be regrouped, testing both cells and plasma; if necessary, the Rh group of the cells should be determined. (iv) The cells should be tested against the recipient's serum, using the pre-transfusion sample of the latter when available. (v) The titre of the agglutinins in the donor's plasma should be estimated if necessary.

(*b*) *The Recipient's Blood (Post-transfusion Sample).*—(i) The sample in the sterile tube should be submitted for bacteriological examination. (ii) The serum from the second clotted sample should be examined by naked eye for the presence of haemoglobin or excess bilirubin. If there is no obvious pinkness the serum should be examined spectroscopically. The amount of bilirubin or the icterus index should be estimated, and Schumm's test for methaemalbumin should be applied. The examination of the pre-transfusion sample, when available, is a valuable control. A small amount of serum should be reserved for serological tests. (iii) The oxalated sample should be divided: one-half should be centrifuged, so that the plasma can be examined for pigments as a check on the examination of the sample of serum; the other half should be kept for serological tests. (iv) *Serological Tests.*—(*a*) A suspension of the recipient's blood should be prepared by adding one drop of blood to approximately 2 c.cm. of isotonic sodium citrate or saline (to make a 2% suspension approximately). This suspension should be examined under the low power of the microscope for the presence of agglutinates. With experience it is possible to recognize the difference between weak diffuse clumping due to auto-agglutination and the presence of small scattered well-formed agglutinates lying in a field of free cells, the latter appearance being due to the presence of clumps of donor cells in the suspension. (*b*) The blood should be regrouped, testing both cells for agglutinogens and serum (the latter from the clotted sample) for agglutinins. If necessary, the Rh group of the cells should be determined and the serum examined for the presence of anti-Rh agglutinins. (*c*) The agglutinins in the serum should be titrated for comparison with the results of titrations carried out on samples obtained later and on the pre-transfusion sample (when available). As explained above, characteristic changes occur after the transfusion of incompatible blood, and if a sample of the donor's blood is not available, or if there is any question of the faulty labelling of a bottle so that the true donor is not known for certain, this investigation may be invaluable. (*d*) If necessary, differential agglutination tests should be carried out.

Note on Methods of Differential Agglutination.—Application of the technique of differential agglutination permits the recognition, in a sample of blood taken from the recipient, of foreign red cells derived from a previous transfusion. The donor cells can be recognized either by being agglutinated by a test serum which does not agglutinate the recipient's cells, or by their failure to be agglutinated by a test serum which completely agglutinates the recipient's cells. For example, when the donor is Rh-positive and the recipient Rh-negative, by testing with an anti-Rh serum the donor's cells (if surviving) can be recognized as discrete clumps lying in a sea of free cells. Alternatively, when the donor belongs to group O and the recipient to group A the recipient's cells can be completely agglutinated with an anti-A serum and the free (donor) cells can then be counted in a haemocytometer. Many further possibilities of differentiation are available if anti-M and anti-N test sera are also used.

Application of the method of differential agglutination is practically essential for the solution of many transfusion problems, but reliable results can only be obtained with considerable experience. For a description of methods see Wiener (1942) and Dacie and Mollison (1943).

(*c*) *Sample of Recipient's Urine.*—The urine should be examined by naked eye and its colour noted; it should then be examined spectroscopically for oxyhaemoglobin and methaemoglobin. If the supernatant fluid contains no pigments a sample should be centrifuged and the deposit examined for the presence of pigment casts. The urine should also be examined for the presence of urobilin (Schlesinger's test). The usual tests for specific gravity and for albumin should be carried out and the reaction determined.

(The concluding part, with case reports and a list of references, will appear in next week's issue)

THREE CASES OF PROLONGED FAECAL FISTULA FOLLOWING OPERATION FOR APPENDICITIS

BY

P. T. CRYMBLE, F.R.C.S.

Professor of Surgery, Queen's University, Belfast

A slight temporary faecal fistula following the removal of a gangrenous or perforated appendix is not an uncommon occurrence, but in our experience it closes naturally in a few weeks. One may look for it in those cases in which the inflammation has spread on to the wall of the caecum, or in which closure of the appendix stump has been unsatisfactory. In the past 15 years three persistent and complete faecal fistulae following appendicectomy operation have been encountered, the duration being one, three, and four and a half years. Once the fistula had become established no motions were passed by the normal route, there was marked incapacity for work, and the social result was appalling.

Case I

The first case was that of a child of 6 who was brought to Queen Street Children's Hospital 15 years ago. The child was wasted, anaemic, in a filthy condition, and had been confined to the house for a year. Its condition did not permit of attendance at school. There was a history of two operations—one for removal of the appendix, with drainage of an abscess; and a second one for the cure of an incisional hernia. It was after this second operation that the faecal fistula appeared.

On examination we found the ileo-caecal valve opening on the surface of the right iliac fossa and discharging squirts of fluid faeces. The entire caecum appeared to be absent, and it was decided that a local closure was impossible. After some building up, the abdomen was opened through the left rectus, and a diversion route established in the following way: terminal ileum divided, and both ends closed; transverse colon divided, and both ends closed; lateral anastomosis between the proximal end of the ileum and the distal end of the transverse colon.

As a result of this severe operation the child had a stormy period of five days, but recovered, and was left with a mucous fistula in place of a faecal fistula. The child returned home, put on weight, recovered strength, and was able to attend school. She attended occasionally at the out-patient department, but one was inclined to postpone the removal of the isolated bowel for some years. However, our hands were forced, as some six months after her diversion operation she walked into the out-patient department with the entire ascending colon prolapsed through the fistula and hanging down under her skirt. She was admitted to hospital, the fistula circumcised, and the terminal ileum, ileo-caecal junction, and ascending

colon removed. The operation turned out to be extremely easy, as the bowel had already mobilized itself. A few vessels were ligatured and divided and the isolated bowel was removed. There was no reaction, and the wound healed in one week.

The specimen was mounted, and is in the Queen's University museum. It shows a very atrophic terminal ileum (usually mistaken for an appendix by the students in the final examination), the fistulous opening surrounded by a ring of skin and the ascending colon (Fig. 1).

FIG. 1.—The terminal ileum, caecal fistula, and ascending colon removed from a child aged 6 years. Note the atrophic terminal ileum and the almost complete absence of the caecum.

Case II

A young man aged 19 was admitted to the Royal Hospital on Feb. 14, 1937, with a faecal fistula in the right iliac fossa which had been present for three years. A gangrenous appendix had been removed in March, 1934, and a drainage tube had been left in for nine days. The faecal fistula followed the removal of the tube, and persisted. His general condition was quite good, and he was under the impression that a faecal fistula was the usual result of the operation he had undergone. He came to the Royal because he desired to join one of the Services, and had been told that he could not be accepted in his condition. All his motions passed by the fistula, but he kept reasonably clean by packing wool into the opening. Examination of the fistula revealed that it was large bowel, and it was thought that a local closure might succeed.

Technique of Operation.—Fistula circumcised and closed by suturing the skin edges together. Clean towels, gloves, and instruments supplied. Peritoneal cavity opened and caecum separated from the anterior abdominal wall. Narrow-bladed Schoemaker clamp applied to long axis of caecum and the muco-cutaneous tissue distal to the clamp removed, leaving a cuff of bowel wall distal to the clamp. The cuff was then sutured, the clamp removed, and the suture line enfolded.

The wound healed by first intention. The patient had a natural motion on the fifth day, and left hospital on March 3, 1937, with a normal alimentary canal. It was fortunate in this case that there was enough caecum left to permit of closure without in any way obstructing the ileo-caecal valve.

Case III

This case was that of a young unmarried woman aged 19 who had passed nothing by the rectum for four and a half years. In June, 1937, after an operation for appendicitis, a faecal fistula developed, and since then no faeces had ever passed by the rectum. In 1939 three attempts were made to cure the condition, but they were unsuccessful. The first attempt was a lateral anastomosis between two loops of ileum, but this produced no change in the fistula. In the second the two bowel loops distal to the anastomosis were divided and closed, but again with no improvement. (These two operations were presumably done under the impression that the fistula was purely ileal, and involved a portion of bowel some distance from the valvula coli.) The third operation was a direct attack on the fistula, and as it caused complete intestinal obstruction it had to be reopened. She left hospital in fair condition with a complete faecal fistula.

On Jan. 14, 1941, she was admitted to our unit with a history of having four fluid motions daily. She had done no work,

FIG. 2.—The right side of the abdomen in Case III. Note the extensive area of ulcerated skin surrounding the large fistula. Three weeks after the short-circuit operation this skin was entirely healed.

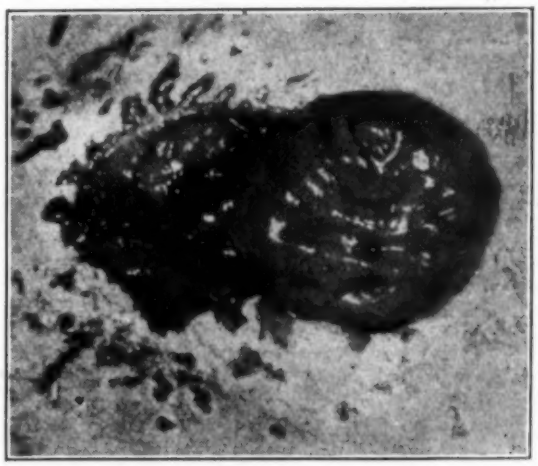

FIG. 3.—An enlarged view of the faecal fistula in Case III. The medial half of the fistula consisted of the prolapsed end of ileum. The lateral half was mainly colonic mucous membrane. Note the ulcerated skin.

but led a fairly normal life. She walked and went to the pictures. There was no emaciation, but she was pale in colour. The whole right iliac fossa showed a skin stippled with small ulcers and areas of white (Figs. 2 and 3). The actual fistula was a complicated arrangement of openings surrounded by a very tender cutaneous margin. The medial half was occupied by the prolapsing end of small bowel (ileum), which discharged no faeces and no gas. The entire index finger could be inserted into it. The lateral half showed two openings, both of which discharged faeces. The upper one could be seen, and it could

be explored with the finger. Its mucous membrane was much paler than the ileal mucous membrane and had the appearance of colonic mucosa. The lower one was too tender to permit examination, and we were uncertain whether it was large or small intestine. Medial to the fistula were two incision scars, one midline and the other right rectal.

Rectal examination revealed a plug of mucus in the ampulla. The patient wore a colostomy belt, which included a large celluloid cup. She was very depressed, had no hope of cure, and showed little enthusiasm for further operative treatment.

Procedure.—The first point was to establish the nature and anatomy of the bowel distal to the fistula. One wanted to be certain that the bowel, which had not been used for four and a half years, was patent, and that the pelvic colon was not involved in the fistula. Olive oil was injected into the rectum and escaped from the two lateral fistulae. Two days later a water enema escaped from the same two fistulae. An opaque enema was then given, and this outlined the colon up to the middle of the ascending colon. It showed a bowel narrow but otherwise normal (Fig. 4). On Jan. 21 the abdomen was

FIG. 4.—Opaque enema of the third case of faecal fistula. The whole colon up to the hepatic flexure is outlined. The pelvic colon has no connexion with the fistula, and the transverse colon is very narrow. This colon had not functioned for four and a half years.

opened through a left rectus incision. No adhesions were found in this region, and there was no difficulty in tracing the small bowel from the beginning of the jejunum to that part of the lower ileum which was adherent to the region of the fistula. This portion of the ileum was divided and the two ends closed. The transverse colon was then withdrawn. It was somewhat small and atrophic, and the great omentum was reduced to a short apron about two inches long. The transverse colon was divided to the right of the middle line and the two ends closed. A side-to-side anastomosis was carried out between the proximal ileum and the distal transverse colon.

Post-operative Course.—Small quantities of fluid were given by the mouth, and there was constant vomiting for five days. On the 25th she had 53 oz. by mouth and vomited 26 oz. On the 26th she had 38 oz. by mouth and vomited 14 oz. The pulse remained good, and ran between 84 and 100. There was slight evening pyrexia. Constant lower abdominal pain was felt, and the patient remained depressed and irritable.

The fistula was dressed for the first time on the 25th, and was found to be covered with a quantity of faeces. It was thought that this had been extruded from the isolated bowel. The lower abdomen was somewhat distended. On the 27th a little flatus was passed, the pulse and temperature had fallen, the abdominal pain was much less, and the patient for the first time was cheerful. Subsequently the left rectus incision discharged a little faeces for a few days, but it had completely closed by Feb. 5. This was an indication that the ileo-colic anastomosis had leaked. At first there was no control over the rectal discharge, but rapidly control was regained, and by Feb. 7 there was normal control of the sphincters. She left hospital in good condition on Feb. 25. The left rectus incision was healed. The skin around the fistula was free from ulceration, and the fistulous area had contracted and was discharging a little mucus.

Lessons from these Three Cases

1. All were cases of the "late appendix" which required drainage, and the condition would never have arisen if the appendicitis had been diagnosed in the first twenty-four hours.

2. If drainage is necessary, never use anything more rigid than a strip of corrugated rubber or a little piece of gauze. A rigid piece of rubber tubing left in for nine days may quite easily perforate the wall of the caecum.

3. Great care must be exercised in handling inflamed or adherent gut, as it is quite easy to tear or rupture such intestine. If the search for the appendix endangers the gut, it is better to leave the appendix *in situ* and content oneself with drainage.

4. It is remarkable how well a patient may be without the use of the colon. The man aged 19 was in excellent condition, and was well enough to desire to join one of the Services. He was not even depressed with his condition, and kept himself reasonably clean with a large plug of cotton-wool packed into the ascending colon. The woman (Case III) was in fairly good health, and, apart from the fact that she did no work, led a normal life. The surrounding skin in her case was a constant source of trouble.

5. Local closure should only be attempted when the fistula involves the caecum or ascending colon and is some distance away from the valvula coli. For example, the planned caecostomy is the ideal one for local closure.

6. In the presence of multiple openings or where the fistula is close to the valvula coli, one should sacrifice the whole right colon and ileo-caecal region by carrying out a two-stage operation: first a diversion operation, and later a right colectomy.

7. In Case III the essential points were the condition of the colon distal to the fistula and the condition of the small bowel proximal to the fistula. The first point was settled by the injection of olive oil into the rectum (this showed a clear route between the rectum and the fistula) and an opaque enema (which showed non-involvement of the pelvic colon). The second point had to be demonstrated at operation. Had there been numerous adhesions in the left side of the abdomen one might have found it impossible to determine the upper from the lower end of a coil of bowel. Fortunately there were no adhesions, and this problem did not arise.

Classification of Faecal Fistulae

(*a*) Slight temporary fistulae following appendicitis operations.—These require no treatment, and tend to heal in two or three weeks.

(*b*) Fistulae following bowel resection.—These arise at the anastomosis or at the closed bowel end, are usually partial, and close naturally. It is easier for the faeces to pass along the mucous channel than to overcome the fibrotic contraction of the fistula.

(*c*) Injury to bowel during operations on adjacent viscera.—Long-standing gall-bladder or kidney disease may lead to adhesions and weakening of the bowel wall. The removal of the gall-bladder or kidney may leave a weak area of bowel wall unsupported, or the bowel may be injured by the surgeon's manipulations, with the result that a few days after the operation a fistula develops. In one case in which the duodenum was involved death resulted. In a second case the ascending colon gave way after the removal of a very adherent tuberculous right kidney. This fistula closed naturally, but was succeeded by a purulent discharge of some months' duration.

(*d*) The operation of caecostomy.—This can be closed by a local operation when the distal route has been restored.

(*e*) The gross permanent fistula involving the caecal wall, some distance from the valvula coli, following an appendix operation.—This is suitable for local closure as in class *d*.

(*f*) The gross permanent fistula in the immediate neighbourhood of the valvula coli or the fistula with several openings.—This should be treated by a two-stage operation. In stage 1 a short circuit is performed by dividing the ileum (as low down as possible), dividing the transverse colon (closing the distal end), and performing an end-to-side anastomosis between the proximal ileum and the distal transverse colon. This converts the faecal fistula into a mucous fistula. In stage 2 a right colectomy is performed.

Conclusion

A final word of warning with regard to purulent or faecal fistulae in the region of the terminal ileum is that there is a tendency for some of these patients to develop small-bowel obstruction after even slight abdominal operations. They would appear to be balanced on the threshold of obstruction, and are pushed over the edge by any manipulations in that region. It is possible that such catastrophes would be avoided by a preliminary short circuit between the ileum and the transverse colon.

COMPLACENCY IN RESUSCITATION OF THE DROWNED

BY

F. C. EVE, M.D., F.R.C.P.

The manuscript directions for resuscitation by the Schäfer method are in the hands (copyright) of the Royal Life Saving Society, who still regard the method as completely adequate. But knowledge of the very intricate subject of respiration has naturally advanced much since Schäfer's day, and an attitude of complacency will cause us to drift behind other countries. An excellent paper by Surg. Lieut. G. H. Gibbens (1942) has given us a useful jog. He had been bitterly disappointed with Schäfer's method when he used it in his ship on drowning cases—now so urgent a problem. Instead of the normal elastic inspiration on removing pressure to which he was accustomed in normal subjects, the victim's abdomen and thorax "felt like putty." Schäfer's method relies for inspiration on elastic recoil, and this was absent owing to lack of muscular tone. He therefore adapted to ships my rocking method (Eve, 1932), in which a dozen times a minute the patient (lashed to a stretcher) is rocked, face downwards, through a total angle of 60 to 90 degrees on a pivot—provided either by a trestle or by a rope from hammock hooks passed under the middle of the stretcher. On this see-saw the weight of the abdominal contents pushes and pulls the diaphragm alternately up and down by a piston action which is actuated by gravity and does not depend on elastic recoil for inspiration. The ventilation thus secured is quite adequate, and is equal to Schäfer's in the normal subject (Killick and Eve, 1933). The air can be felt, and heard, passing in and out freely; there is no need for voluntary breathing. A manual method is used till rocking has begun. On shore, a builder's two-wheel hand-cart would do well for rocking. Prof. Cordier of Belgium points out that in Scandinavia and Eastern Europe Silvester's method—in spite of its disadvantages—is considered more efficient, especially when tested on the warm cadaver which is toneless. They advance excellent reasons for this preference, which are too lengthy to quote here.

Schäfer's Method

On reading Schäfer's (1907-8) splendid Harvey lecture I see that he started experiments in the dead-house, but found rigor mortis an insuperable difficulty; warm cadavers are not mentioned, nor are drowning cases. Then he proceeded to anaesthetized dogs (drowned) and afterwards to normal humans. Speaking of his method, he says that you should "press gradually for three seconds with both hands close together flat on the back over the loins, the fingers extending over the lower ribs. . . . Of course, on relaxing the pressure the same volume of air must pass in again as the chest resumes its former shape and size."

Unfortunately, this perfectly natural assumption, justified by his experiments on normal people, does not hold good in the nearly drowned, in whom the elastic tone of the respiratory muscles fails progressively. Later, he modified his directions so as to compress the diaphragm only; but with large hands and small loins the ribs cannot always be avoided—neither, in my opinion, can it be an important point when fighting to save a life.

Other Imperfections of Schäfer's Method

The fact is that Schäfer's method has many well-known advantages and may be the best manual method; but it is not a perfect method, and it is deplorable complacency—especially in these days of U boats—not to make every effort to find a better one. We must think not so much of the very numerous successes of Schäfer's method but rather of the distressingly greater number in which it fails, and try to diminish this. A drawback of Schäfer's method is that the weight of the shoulders and upper back opposes inspiration. This, in other countries, has been met by a second operator, who lifts the folded elbows (arms extended high over the head) upwards from the ground during inspiration—thereby greatly improving ventilation and circulation (Hederer). Radiographs have recently shown (Barclay) that in the prone position the diaphragm is pushed up into the full expiratory position, and this second drawback would be increased in the toneless body. This is partly countered (Henderson, 1937) by extending the arms above the head, but both of these methods rely on muscle tone.

The main defect in the nearly drowned is muscular tone, both for circulation and for respiration. It is therefore useless to judge any resuscitation method by its effects on normal persons: the best criterion is the toneless warm cadaver, and I have rocking stretchers at various hospitals to test this aspect.

Tone of the Diaphragm

The diaphragm is the chief and only indispensable muscle of respiration. It achieves inspiration by contracting its high dome into a low dome. In the warm cadaver, as it has lost all tone, the diaphragm is pulled fully up by the elastic contraction of the lungs, and by the pressure of the abdominal contents.

In the semi-final stages of incomplete death, of the three methods of resuscitation Schäfer's will be the first to become impotent with the loss of elasticity (due to tone of the diaphragm), on which he relies for inspiration; Silvester's method will still have some elastic recoil around the ribs to rely on; the piston action of my rocking method should work even more freely as the tone of the diaphragm declines. How swiftly this may happen was shown by H. W. Haggard (U.S.A.), who tried artificial respiration on a man who had just had a fatal heart attack. Ventilation of the lungs was normal at first, but after 10 to 15 minutes it failed completely. The asphyxiated nerve cells of the bulb and spinal cord which maintain the muscles in tone had died, so that the lungs collapsed in the toneless thorax. Henderson (1937) demonstrated another instructive point by measuring the total air respired in a quarter of an hour by various students. Then he tried artificial respiration on them and found the same figure, however hard the operator tried to increase the ventilation of the lungs. The respiratory centre—amazingly sensitive to CO_2—knew exactly how much ventilation was necessary, and by modifying the tone of the diaphragm set the stroke of its piston to give the correct ventilation both in natural and in artificial respiration.

Attempting Better Methods

The trouble with apparatus for the rocking method is that it may not be at hand when needed; but, in a ship, a stretcher which can be rocked could be instantly available, and if resuscitation drill is practised the interval between the victim's lying on the deck and rocking on the stretcher will already have been reduced—with my later gadgets—to 25 seconds. I find, from the officer responsible for first aid in one of the small ships (a mine-sweeper) which carry out many of the rescues from drowning in convoy, that there is no difficulty—as he showed me—in storing, suspending, and rocking a stretcher; he was enthusiastic about it. The short boat journey to the ship is the weak but vital stage. Thwarts and crowding may render the Schäfer method impossible in a boat. So our St. John men at Beverley are trying rocking each other on the four bent forearms of two men (opposite), with their two pairs of legs steadied by a thwart between them. Improvements

need working out; e.g., for the two operators to grasp mutually a pair of rings like deck quoits: suggestions are welcome—if tried out. When the method, even in its provisional form, was tried on me in a ship's lifeboat it seemed quite effective. Mr. Akrill, our local first-aid expert, whose help has been invaluable, has to his credit a resuscitation from drowning after 70 minutes of artificial respiration by alternate Schäfer and Silvester—aided by epigastric pushes in expiration, which would help both heart and diaphragm. This seems an excellent plan, for if the current of air at the mouth is not satisfactory by one method you should try another. A local unsuccessful case (by Schäfer only) was that of a short stout woman from whose lungs a pint and a half of water had first been emptied. Such people already have a high diaphragm, and in the prone position her heavy weight pressing on her prominent abdomen would force it higher still. Silvester's method might well have been better for her. Schäfer's method does not always drain away the water as alleged, for in a Hull child recently the water merely bubbled to and fro. Water in moderate amount is quickly absorbed from the lungs into the blood. Drowning cases always suffer from shock, so that in the U.S.A. they are resuscitated in the head-down posture—say 10 degrees—if sloping ground allows. Gibbens points out that this would impede inspiration, but it should help the heart—probably more important.

Other Respiratory Aids

In its very complete review of "breathing machines" the Medical Research Council (1939) states: "For short emergencies we would recommend insufflators of the Oxford or the McKesson type actuated by oxygen pressure and a tilting stretcher based on the Eve principle, which is almost foolproof and needs little attention; its use is a simple extension of instruction in manual methods of artificial respiration. It is therefore particularly valuable in industrial establishments and places where respiratory accidents are frequent." Gibbens (1942) has shown its adaptability to ships. Messrs. Siebe Gorman are (presently) making to my design a simple latticed metal stretcher in which bandaging is nowhere impeded by canvas. If desired it can be rocked, and the rock is reinforced by a jerk—whereby the momentum of the moving viscera and blood columns is valuably enhanced.

The respiratory centre judges the need for deeper respiration by the minutest increase of CO_2 in its blood. Hence inhalation of CO_2, preferably 5 to 8% in O_2, is a potent respiratory stimulant, telling the centre to cause deeper breathing so as to wash out of the lungs the unnatural excess of CO_2. The Novox apparatus is efficient for this purpose, its tube being led via the pivot of the stretcher.

Warmth.—The value of this in shock is well known, and every drowning case is shocked. Heat production is therefore minimal and heat loss very serious, especially in a cold wind and from the evaporation of wet clothes. Hence, besides blankets and hot-water bottles, impervious coverings such as waterproofs are very valuable. Heat loss can only be visualized by the imagination, and even nurses often fail to perceive it. Always we must bear in mind that in resuscitation it is the nerve cells of the respiratory (and spinal) centres which we have to revive with warm circulating blood, oxygenated by moving lungs. With circulation vastly enfeebled the neck and its vital nerve cells may rapidly be chilled. I (Eve, 1900-1) found that the sympathetic nerve cells of the rabbit were killed by a temperature of 50° C., and were paralysed, till re-warmed, by cooling 20° C. below blood heat. High-grade nerve cells should be still more sensitive to cooling, and their blood vessels may be constricted by chill, so that it seems well worth while to apply a rubber hot-water bottle to the cervical spine as soon as Schäfer or rocking has started. A. T. Cholerton writes (March, 1943) from Moscow: "In this winter offensive, even a lightly wounded man, if left lying, dies of frost-shock in 10 to 30 minutes.

Another argument for warmth—to the chest—is that plain muscle, with which the lungs are well supplied, contracts with cold and relaxes with warmth. This is evident in many parts of the body, conspicuously in the scrotum and veins of the hands. Hence the lungs should shrink when chilled externally or internally by cold air and evaporation from redundant ventilation. Warmth should relax the lungs and assist inspiration.

It would be valuable to compare the statistics of successful resuscitation after drowning in cold seas and warm. In Australia there were for ten years no failures in resuscitation on bathing beaches patrolled by the Australian Surf Life-Saving Association. Rescues were prompt and a modified Schäfer's method was employed. But I have seen pictures of these fine young men carrying also a rocking stretcher.

Heart and Circulation

The very important needs of the heart and circulation are not studied enough here. In the U.S.A., Henderson (1937) considers that hypotonia is the essence of shock, and he finds that when, as in drowning, the tone of the muscles is lost the heart fails because it does not get enough blood from veins unsupported by muscle tone. Obviously an empty pump can't work. This theory rings true to me, and I see no inadequacy in it (as he does). For let us substitute—for the heart and artery, veins, and capillaries of the leg of a standing person—a rubber pump and a long vertical rubber U-tube with some cotton-wool in the bottom of it to imitate the capillary resistance. The model will work all right unless the venous return half is replaced by thin-walled tubing, which the blood will distend and in which it will stagnate without reaching the heart. Even if this model is laid horizontally in bed its arterial side will be ill filled (and thus low-pressured) until the "heart" is filled by raising the bed-foot. Similarly, the venous return to the actual heart will fail when the veins and capillaries are deprived of their external support by the muscles universally losing their tone as they do in drowning. Schäfer's method is helpful here because incidentally it squeezes venous blood from the abdomen to the heart. The well-intentioned efforts of first-aiders to stroke venous blood from the limbs appear to me rather fatuous. In this respect the rocking method should be pre-eminent, though the point should by proved by the physiologists; for while gravity will propel the venous blood alternately from the legs and the extended arms towards the heart, the valves in the veins and right heart will prevent the return current. Similarly, the alternating pressures in the chest fill and empty the pulmonary blood into the left heart. The accompanying diagram clarifies

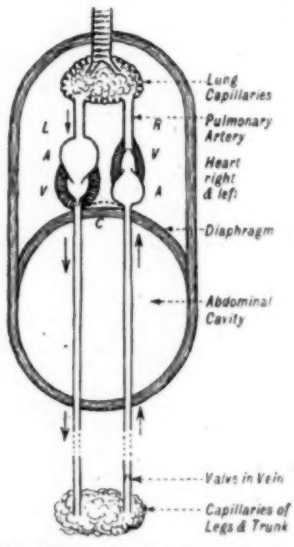

Diagram analysing the effects of rocking on the two circulations

the various valuable effects of rocking on the two circulations and the coronaries. Smart but slow rocking (10 to 12 a minute) is probably best for the circulation. As you rock try to visualize the flow of blood in the long veins and arteries.

Anaesthetists find (personal letter from Mr. G. H. Colt) that the stopped respiratory centre seldom restarts working unless it is congested; in the rocking head-down posture one can see and feel congestion in the head. This may also restart a stopped heart.

Conclusions

Artificial respiration is a very misleading and therefore, maybe, a life-losing name. For resuscitation is not a simple

matter of ventilating the lungs; it is a trinity of *ventilation, circulation,* and *warmth.* Essentially it is an attempt to revive asphyxiated *nerve cells* in the medulla and spinal cord by a circulation of warm blood oxygenated by moving lungs.

Ventilation.—When asphyxiated by failure of respiration or circulation these nerve cells gradually die—usually in a few minutes, but they may remain viable for an hour, rarely more. When they are dead all hope is gone. As they die, the elastic *tone* of the muscles—which they maintain—progressively declines. When the diaphragm has in this way lost all its tone the lungs contract by their own elasticity; they pull the diaphragm right up and become deflated (as in the warm cadaver). At this stage (1) Schäfer's method has become impotent because the elastic recoil of the diaphragm (for inspiration) has gone; (2) Silvester's method will still produce some ventilation owing to elasticity in the thorax independent of its pectoral muscles; (3) the rocking method will effectively shift the flaccid diaphragm up and down independently of tone, and hence should save cases in which loss of tone had gone too far for the Schäfer method to revive.

Circulation.—The heart muscle itself does not die quickly, for after drowning it can be revived by perfusion with oxygenated saline solution—a baby's heart after several hours. The diagram shows how well the head-down tilt perfuses the coronaries. But in shock (hypotonia of muscles) the heart may also fail from mere emptiness because insufficient venous blood gets back to it through veins and capillaries unsupported by tone of muscles. Hence in drowning cases (always shocked) it is important to encourage venous return, as by the compression of abdominal veins which occurs in Schäfer's method or, far more potently, by the rocking method—as already explained. To fill the heart and respiratory centres with blood a head-down slope of about 10 degrees (1 in 6) should be chosen (as on a beach) for manual resuscitation when possible. To fill an empty heart is a quick way to restart it beating. When you tilt steeply to empty out water you incidentally fill the heart and change the coronary blood.

Warmth.—This is indispensable in shock treatment generally—e.g., by hot-water bottles and blankets; also by impervious coverings, to prevent heat loss from evaporation and cold winds. Nerve cells are paralysed by cooling but revive at once on re-warming. With a crippled circulation the indispensable nerve cells in the upper spinal cord will quickly cool and their blood vessels constrict. Hence it may prove very important to warm the back of the neck by a rubber bag early in the resuscitation.

Finally, transcending all else, it is essential to start Schäfer's method instantly: if ventilation (checked at the mouth) is satisfactory, persevere; if not, try Silvester plus expiratory pressure on the upper abdomen, or, better, proceed to rocking if available.

Confronted with so many lamentable failures of Schäfer's method our Naval medical officers seem entirely justified in advising for preference the rocking method, which is now included in BR 25/43, "First Aid in the Royal Navy."

Explanation of the Diagram

Since gravity in rocking affects only the longitudinal components of the blood vessels they may be represented as straight tubes. For clarity, the vessels of the arms (extended on the stretcher handles) and head are omitted: they are similar to the legs. Natural circulation is assumed to have stopped. The piston of this air-pump is formed by the weight of the abdominal viscera (capped by the flaccid diaphragm) sliding up and down. The patient is prone on the rocking stretcher.

When *head-down,* venous blood from the legs and abdomen falls past the right heart into the lung capillaries—reflux prevented by valves in the right heart and leg veins. Veins in the head and extended arms fill. The right heart fills (which may restart it). The aortic valves are banged shut by a pressure of 2 to 3 feet of blood: hence blood is forced into the coronary arteries and joins the stream flowing from the right heart into the lungs (course indicated by the dotted line C).

When *feet-down,* the venous blood which has just been oxygenated in the lungs cannot flow back into the right heart or into the legs (valves closed), but is free to flow past the open aortic valves into the leg capillaries. Blood from head and extended arms refills the right heart.

Thus analysed, slow rocking appears able to aid, or even to maintain unaided, both circulations in the drowned—including the all-important coronary circulation. Silvester's method—unless the epigastrium is compressed—seems to be ineffective on the circulation: Schäfer's method should push some abdominal blood into the lungs but perhaps no further.

My grateful thanks are due to Surg. Lieuts. G. H. Gibbens and D. de Launay, R.N.V.R., for their helpful collaboration and to Prof. R. Hemingway on the physiological side. Also to Mr. Akrill and the Beverley Division of the St. John Ambulance Brigade, and for the use of their hall for experiments.

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BLAST INJURY TO THE ABDOMEN BY DEPTH CHARGE

BY

D. DENHAM PINNOCK, M.B., F.R.C.S.
Lieut.-Col., R.A.M.C.

AND

PAUL WOOD, M.D., F.R.C.P.
Lieut.-Col., R.A.M.C.

As little information has been published concerning the effects of blast injury to the abdomen the following cases are recorded in order to supply additional data. Under conditions of active service it is not possible to do justice even to the very scanty literature. However, it can be mentioned that, in Zuckerman's (1940) experiments on animals exposed to air blast, haemorrhagic pulmonary lesions were the chief feature, and that according to Hamilton Bailey (1942) blast injury to the abdomen may be followed by melaena. That author also states that, although laparotomy has been performed with negative findings on several occasions, rupture to the colon has been revealed by timely operation. Breden, d'Abreu, and King (1942) record a number of cases of abdominal blast injury from depth charge, and they refer to papers by Atkins (1940) and by Gordon-Taylor (1940). These records show that persons swimming in the water close enough to an exploding depth charge may suffer blast injury to the abdominal viscera, characterized by shock, haematemesis, melaena, and pyrexia; recovery may take place without surgical intervention; perforation of the gut may sometimes be successfully treated by surgical repair; many of these patients have died before conditions were suitable for careful study or surgical help. Associated blast injury to the lungs is common.

In December a naval vessel was torpedoed and sank rapidly. The crew took to the water and were swimming away from the ship when two depth charges exploded in quick succession. Some who had managed to clamber on to rafts escaped all injury; others who had swum further afield felt the shock but suffered no ill effect; while about 15 felt as if kicked in the stomach or pelvis and were sufficiently injured to be taken to hospital. Of these 15, five were seriously ill and form the subject of this report. The other ten did not appear ill and had no symptoms suggesting serious trauma to internal organs; they recovered uneventfully.

The history given by four of the seriously ill patients was very similar (the fifth was more or less unconscious owing to a head injury received on the ship): they were all swimming in the water with their heads out and supported by life-jackets. Three felt as if kicked in the stomach, the other in the back of the pelvis. After receiving the injury they were still able to swim until they were picked up. They were all seen in hospital within four hours of the event.

Case I

This patient had most of his chest out of the water when the depth charge exploded, for he was trying to lift himself on to

a raft. He complained of increasing abdominal pain and had vomited blood, but he developed no pulmonary signs or symptoms.

Examination revealed board-like rigidity with considerable tenderness all over the abdomen, normal lungs, and no fractures or external injuries. His general condition seemed good: the pulse rate was 90 beats a minute and the pulse volume fair. The following day he still seemed fairly well, the haematemesis having stopped and the pulse rate and blood pressure remaining in the region of 90 and 110 respectively, but the board-like rigidity and tenderness of his abdomen had lessened very little. A radiograph of his lungs confirmed the fact that there was no pulmonary blast injury. On the third day it was decided to operate, as his general condition was deteriorating and the abdominal signs were not improving. He was given a pint of plasma before and a second pint during the operation. Laparotomy revealed perforation of the transverse colon with localized peritonitis and two small tears in the peritoneum of the floor of the pelvis. The perforation was repaired and a proximal colostomy tube inserted. The peritoneum was drained.

Rather unexpectedly the patient went steadily downhill, with signs of increasing circulatory collapse, despite repeated infusion of plasma, rectal saline, and fluid by mouth. He died on the fifth day. No necropsy was performed.

Case II

This patient gave the typical history and noted that there was no pain in his chest immediately after the explosion, but that within the next four hours pain around the lower thorax increased steadily. He vomited a good deal of blood and may have coughed up some also.

On examination he was found to be considerably shocked, with a pulse rate of 136 and a small pulse volume. There was board-like rigidity and marked tenderness over the whole of his abdomen, and, although it was thought he had ruptured some viscera, he was too ill for surgical intervention. Repeated infusion of blood plasma and continuous oxygen administration failed to improve his condition, and he died with signs of increasing shock in about 24 hours. No necropsy was performed.

Case III

The history in this case was similar to that of the others: after being withdrawn from the water the man felt increasing pain across the lower thorax and began to cough up blood; there was no haematemesis.

Examination revealed coarse rales over the left lower lobe, with diminished air entry and normal percussion note. There was moderate rigidity of the abdomen, but in less degree than in the previous two cases. The pulse rate was 100 beats a minute, with fair volume. The patient's general appearance was good and he did not look as if he had suffered serious intra-abdominal injury. When seen 24 hours later, however, his condition was worse, shock having increased and signs of injury to the bowel being more evident. There was board-like rigidity of the abdomen with considerable tenderness, but still no haematemesis; haemoptysis was less, but the pulmonary signs were more extensive.

After adequate resuscitation laparotomy was performed and seven perforations of the small intestine were found. The appearance of the gut suggested that many loops of small intestine were severely bruised at the point where they crossed the pelvic brim. There were localized areas of simple bruising, localized areas where bruising had progressed to gangrene, and seven places where a gangrenous section had perforated. In several areas loops of intestine obviously damaged had become stuck together and were not separated; fistulae could well have formed between these adjacent loops. There was widespread peritonitis. Repair was effected by sewing up the perforations and inverting the gangrenous areas that had not yet perforated. The peritoneum was drained, but jejunostomy was not carried out.

The subsequent course was steadily downhill, and was characterized by fever and extending signs of blast-lung, by increasing circulatory collapse—despite almost continuous intravenous infusion of blood and plasma—by complete paralysis of the gut, and by evidence of increasing peritonitis.

After a gallant but hopeless fight the patient died five days after the injury. Necropsy showed extensive haemorrhagic lesions in the lung, with secondary bronchopneumonia, widespread peritonitis, and gross distension of the gut, but no new perforations. A long section of the small intestine was gangrenous, possibly from mesenteric thrombosis following the injury, as no damage to the mesentery was found at the operation.

Case IV

This patient was the only one who received the shock of the explosion in the back of the pelvis, instead of in the stomach. After being dragged out of the water he complained not only of pelvic pain but of increasing raw bilateral lower thoracic pain; he then developed a painful cough with haemoptysis, and each time he coughed it was stated that red blood was forced from the rectum, but the amount was not noted. He tried repeatedly to pass water, but was unsuccessful for four hours, when a catheter was passed with difficulty and normal urine was withdrawn.

On examination he had obvious signs of blast-lung with widespread rales and diminished air entry over the right lower lobe. A radiograph of his chest confirmed the diagnosis and also revealed changes at the left base. In order to avoid further damage the rectum was not examined (what bleeding there was having stopped), nor were there further signs to suggest serious trouble here.

This patient differed from all the others in that his abdomen was soft and not tender. His general condition was good—the pulse rate 90 to 100, with fair volume. He received no special treatment, had no infusion of blood, plasma, or fluid, and made a steady and fairly rapid recovery, so that within 48 hours he was obviously out of danger.

Case V

This patient was unable to give an adequate history owing to the fact that he had received a head injury when the ship was torpedoed and was unconscious in the water when the depth charge exploded. When first seen he was extremely ill, with haemoptysis and physical signs of blast-lung, haematemesis, and board-like rigidity of his abdomen with extreme tenderness. His mental state was confused and drowsy, but there were no localizing signs in the C.N.S. He was badly shocked, and died within 48 hours. He was far too ill to stand surgical intervention. No necropsy was performed.

Commentary

It is not the purpose of this report to discuss the features of blast-lung, but attention is drawn to the fact that in the one patient (Case IV) who had a proved lung lesion the abdomen remained perfectly soft but without gut injury within the peritoneum. Bleeding from the rectum in this case may have been due to damaged haemorrhoids or to small tears in the bowel wall, and it will be remembered that it was this same patient who felt the shock in the back of the pelvis instead of in the abdomen. In contrast, Case I, in which there was a proved gut injury but no symptoms, signs, or radiographic evidence of blast-lung, had marked rigidity of the abdomen. In considering the management of these cases the significance of the abdominal rigidity was questioned, for it has been stated that blast-lung may produce such rigidity. These cases suggest that board-like rigidity of the abdomen should be regarded as evidence of perforation of the gut, and should not readily be put down to blast-lung.

All four patients who had gut injury died, which suggests a worse prognosis than that indicated in the literature described above. When first seen, and for 36 hours afterwards, the condition of two of them was deceptive in that they did not look severely shocked or as ill as one might expect in patients with perforation of the intestine: the facies of moderate well-being was completely unlike the aspect of the common abdominal catastrophe. The rigidity was much more pronounced than we had previously seen in any case of perforation of the intestinal tract; we had only once seen it equalled, and that in a man with rupturing dissecting aneurysm of the abdominal aorta.

That the general appearance was so good misled us to the extent that we were loath to accept perforation as the cause of the rigidity (recollecting what we had read in the Army Medical Bulletin No. 5 of the great rigidity encountered in cases of blast-lung), and the opinion was formed that the condition was due to blast-lung, with probable actual damage to the abdominal muscles. Even 24 hours later, when there was obvious deterioration in the condition of these patients and when operation was decided upon, one of our surgical colleagues remarked that he had not seen a patient with a perforated viscus of so many hours' standing with so good a facial aspect, and could not believe that such a catastrophe had occurred.

It is probable that these patients would have done better with immediate surgical intervention. On the other hand, the lesions

found at laparotomy in Case III make it clear that perforation results from gangrene supervening on gross bruising, and that many patches of bruising do not lead to gangrene and perforation, so that too early laparotomy might defeat its purpose if perforation were to occur subsequently. However, the findings point to the necessity for exploration of the abdomen in cases of this type, and in future one would prefer to explore—even in the early hours—and find nothing more than bruising of the viscera, and would be prepared to operate a second time if a later perforation occurred.

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INTOLERANCE TO LIVER EXTRACT IN PERNICIOUS ANAEMIA

BY

ELIZABETH DELIKAT, M.D.Bratislava

Assistant Pathologist, the Royal Hospital, Wolverhampton

It is a matter of common experience in clinics devoted to the treatment of pernicious anaemia that a certain small proportion of patients treated with liver by the parenteral route in course of time become "sensitive" to the injections. In such cases treatment may successfully be carried on by the oral route; this method of administration of liver extract is, however, extremely wasteful, and the Ministry of Health has made an Order, dated May 21, 1941, under Regulation 55 of the Defence (General) Regulations, 1939, which lays it down that liver extracts shall not be administered otherwise than by injection. At the suggestion of Dr. S. C. Dyke, Director of the Pathological Department of the Royal Hospital, an inquiry has therefore been undertaken into the possibility of inducing patients who had become sensitive to liver to tolerate their requirement by parenteral injection.

Out of about 200 patients with pernicious anaemia attending the department over the past fifteen years 14 were known to have become intolerant to liver by parenteral injection. None of these gave any previous history of allergic manifestations, but in all cases the symptoms of intolerance were those usually associated with allergic hypersensitivity. These ranged from slight local manifestations at the site of injections, such as redness, induration, and itching, through all gradations up to severe constitutional reactions associated with generalized urticaria, vomiting, failure of vision, and attacks of typical spasmodic asthma. In some cases the symptoms were alarming, and necessitated the detention of the subjects in hospital; in the milder cases they responded readily to ephedrine by mouth, and in the more severe to adrenaline hypodermically. It was found that once sensitization had been established it extended to all brands and types of liver extracts; attempts to carry on treatment with preparations other than those responsible for the sensitization were uniformly unsuccessful. In some cases the allergy was only transient; in others it was persistent and had necessitated a change-over to administration by the oral route. Three cases of this latter type formed the subject of this investigation.

Treatment of Three Cases

Case 1.—Man aged 52. Under treatment for pernicious anaemia since May, 1939. Maintenance dosage, 4 c.cm. of liver extract parenterally every six weeks. In Oct., 1940, after the usual injection he developed generalized urticaria, with puffiness of the face and failure of vision; thereafter he was treated with liver extract orally, 1 oz. daily, until Dec., 1941, when it was decided to attempt desensitization. Intradermal tests with 0.1 c.cm. of two different brands of liver extract gave strongly positive skin reactions. The attempt at desensitization was begun with a dose of 0.1 c.cm. of liver extract, which was tolerated well; increments of 0.1 c.cm. were made at each successive dose, given every second day until a dose of 1 c.cm. was reached; thereafter an increment of 0.2 c.cm. was used. The patient attended every third day, and remained in hospital for two hours after each injection until he could tolerate 3 c.cm. of liver extract in one dose. This dose was increased by 0.5 c.cm. at two-weekly intervals until 4 c.cm. could be given in a single injection. The patient now tolerates this dose every four to five weeks, and on it a normal blood picture is maintained. On some occasions after this injection of 4 c.cm. of liver extract he complains of slight headache and shows some swelling of the forehead; this disappears on giving ephedrine. He is admitted to hospital for two hours for each monthly injection; probably it will be possible to dispense with this precaution in the future. The intradermal tests with liver extract are still strongly positive, though less so than before desensitization.

Case 2.—Woman aged 61. Under treatment for pernicious anaemia since May, 1939. On maintenance dose of 4 c.cm. of liver extract parenterally every two months until 1940. In March, 1940, she collapsed after her injection; the same thing happened again in May, 1940. Treated by liver extract orally, at first 1 oz. and later 2 oz. daily. This dose was not enough to maintain a normal blood picture, and in Sept., 1941, it was decided to attempt desensitization. Somewhat surprisingly, skin tests with liver extract gave negative results. For the next five months she was admitted to hospital for one day every four weeks and received her liver extract parenterally in divided doses, starting with 0.1 c.cm., with increments of 0.1 c.cm. every 20 minutes so long as no reaction occurred; on the occurrence of a reaction time was allowed for the symptoms to subside, when the previous dose was repeated. The reactions consisted of tachycardia, vomiting, and malaise; there were never any dermal manifestations. By Jan., 1942, the patient tolerated a dose of 2 c.cm. of liver extract in two injections of 1 c.cm. at an interval of one hour. At this time the state of the blood was not satisfactory, but an attempt to raise the total dose to 2.5 c.cm. resulted in severe collapse. In March, 1942, owing to the unsatisfactory state of the blood picture she was admitted to hospital. She then received 6 c.cm. of liver extract parenterally in divided doses over two days. After a single dose of 1 c.cm. she developed for the first time generalized urticaria, and intradermal tests with 0.1 c.cm. of liver extract were found to be strongly positive. In spite of this she now tolerated a dose of 0.5 c.cm. of liver extract, and a desensitizing course was started from this level with increments of 0.1 c.cm. daily up to a single dose of 1.5 c.cm. This injection, however, again gave rise to generalized urticaria, and had to be repeated the next day, when it was well tolerated. Desensitization was thereafter continued with increments of only 0.1 c.cm. up to a dose of 2 c.cm., and later of 0.5 c.cm. until 4 c.cm. was tolerated in one dose. A total of 34.5 c.cm. of liver extract was given in 21 days. The patient now receives 4 c.cm. of parenteral liver extract in a single dose every four weeks without disturbance.

Case 3.—Female aged 44. Under treatment for pernicious anaemia since Aug., 1940. Maintenance established on a dose of 2 c.cm. of liver extract parenterally every two months. In May, 1940, after her usual injection, she developed generalized urticaria and collapsed. On three more occasions she developed urticaria after her injection. In Jan., 1942, intradermal tests with 0.1 c.cm. of liver extract were strongly positive. This patient has been unable to spare the time for frequent attendances at the hospital, and in her case no serious attempt at desensitization has therefore been made. She attends every six weeks and receives her requirement of liver extract in divided doses, starting at 0.1 c.cm., with increments of 0.1 c.cm. at intervals of 20 minutes until the first signs of intolerance appear; these in this case are flushing of the face and a feeling of tightness of the throat, and usually appear after a single dose of 0.3 to 0.4 c.cm. She then goes home and returns on the following day, when we have found the injections to be well tolerated. Dosage is started at the level reached on the previous day and proceeds at increments of 0.2 c.cm. at 20-minute intervals. The full requirement of 4 c.cm. for six weeks is usually injected in two days.

In all our cases the symptoms of intolerance to liver injections appeared only after several months or years of parenteral treatment; the interval between the injections was at least six weeks, for the reason that no patients under maintenance treatment in this department receive their injections at shorter periods.

Discussion

In view of the facts there is every reason to suppose that the intolerance is an anaphylactoid phenomenon and due to "allergic" sensitization, the liver acting as an antigen. This is the usually accepted view (Criep, 1938; Jones, 1939). Our experience, using different brands and types of liver extract, would lead us to believe that none are free from bodies capable of this antigenic action. Various methods of desensitization have been suggested: splenic extract (Schlesinger, 1930); histamine (Corelli, 1935); "quotientin," which appears to be an empirical remedy alleged to contain hypophysial, parathyroid,

and suprarenal extracts (Lasch, 1936); various preparations of calcium (Lasch, 1936; v. Herff, 1937; Gigante, 1939); liver powder orally in increasing dosage (Diena, 1938); and the parenteral injection of liver extract in divided and increasing dosage (Engel, 1933; Grün, 1933, 1934; Krantz, 1938). This last, in view of known facts as to sensitization and allergy, appears to be rational, and was therefore adopted in this investigation.

That negative skin tests do not exclude intolerance to liver extract is shown by Case 2, in which these were negative 18 months after the onset of symptoms and became positive only during the attempt at desensitization. Two methods may be adopted for the parenteral administration of liver extract to intolerant patients: lasting desensitization can be achieved by a course of liver injections in increasing doses over several weeks; alternatively, the required dose may be given in small injections, preferably over two days. The latter method does not increase the tolerance of the patient to future doses.

Summary

Three cases of pernicious anaemia are described in which the patient had become "sensitive" to the parenteral injection of liver extract.

Skin tests cannot be relied upon to indicate intolerance.

By the use of divided doses of liver extract over a period of several weeks it proved possible to desensitize two patients to the extent that they became able to tolerate their full requirement of liver extract in one injection at monthly intervals. In a third case the required dose is being given in small injections over two days without attempt at permanent desensitization.

My thanks are due to Dr. S. C. Dyke for access to records and advice, and to Sister Dora Martin for care and supervision of the patients while in the wards.

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Medical Memoranda

Irritation of the Urinary Tract by "Doped" Beer

On the afternoon of Oct. 6, 1942, two ratings reported sick on board, one with the clinical features of acute pyelitis and the other with those of acute anterior urethritis. Provisionally these were regarded as infections with *B. coli communis* and the gonococcus respectively, and in both cases treatment with sulphapyridine and alkalis was instituted. There appeared, however, to be something unusual about these cases. First, acute pyelitis is an uncommon condition in young men; and, secondly, the rating with urethritis had a temperature of 102° F., with only a very slight mucous discharge. This pointed to the possibility of some causative factor common to both, and on close questioning it transpired that these two men and a companion had on the previous afternoon visited a brothel when the ship had put into port for a few hours. There they had had some beer, which, though it tasted normal, probably contained an aphrodisiac of the nature of cantharides, which had acted as a violent irritant of the urinary tract. It is known that for business purposes the proprietors of brothels do "dope" their drinks in this way, and naval personnel are advised never to quench their thirst at such places.

The third rating in the party complained of no symptoms whatever, and subsequent microscopical examination of his urine revealed no evidence that he had been affected. The stories of all three, however, combined to make it clear that he had drunk much less beer than his two companions, and that the one with pyelitis had had considerably more than the one with urethritis. There was thus a fairly close correlation between the amount of suspected beer consumed and the severity of the subsequent symptoms.

CASE RECORDS

Case 1.—Able Seaman "X," aged 22, reported sick on Oct. 6, 1942, complaining of severe pain in the penis at the end of micturition during the past few hours; he was passing water about every half-hour with some urgency. Aching pain was also felt across the loins, spreading down the back of the thighs into the calves. Frontal headache and nausea were present. He had never had a similar attack in the past nor any other urinary trouble. Examination showed: temperature 103° F.; tongue furred; tenderness in both loins and over the pubes; neither kidney palpable. The urine was cloudy, with a naked-eye deposit of pus on being left to stand. (Microscopy was not possible until two days later.) Progress was as follows: Oct. 7: Restless the previous night and vomited four times. Morning and evening temperatures 99.2° and 98.4° F. respectively. Frequency becoming less. Oct. 8: Pain now present during whole act of micturition. Nausea and generalized abdominal discomfort. Tender in both renal angles. B.P. 110/80. Urine clear to naked-eye inspection, but many pus cells and an occasional red cell seen on microscopy; no casts or organisms seen. Oct. 9: All symptoms diminished, but back still weak. Developing herpes labialis. Some pus cells and an occasional red cell present in urine. Oct. 14: Return of pain in the back and painful micturition. Temperature up to 101° F. Tender in loins, above Poupart's ligaments, and over pubes. Many more pus cells present in urine. Oct. 22: Patient completely recovered; symptomless; no pus cells visible even in a centrifuged specimen.

Case 2.—Able Seaman "Y," aged 24, reported sick on Oct. 6, 1942, complaining of pain in the penis on micturition during the past few hours; pain worse at the end of the act; a little frequency but no urgency. Intercourse the previous afternoon and five days before. No history of similar trouble or of venereal disease in the past. Examination revealed a temperature of 102° F. and very slight mucous discharge from urethra. (A smear taken before starting treatment with sulphapyridine was subsequently shown to contain a very few pus and epithelial cells only—no gonococci.) Progress was as follows: Oct. 7: Passed water four times the previous night; complaining of nausea and dizziness; temperature normal all day. Oct. 8: Appetite returning; pain during micturition still present; no urethral discharge. Many pus cells seen in urine on microscopy. Oct. 9: Urine contained a few pus cells. Oct. 11: Feeling well; symptomless; only a very occasional pus cell seen in urine.

COMMENT

One case each of acute pyelitis and acute anterior urethritis are described, both suspected of being due to an aphrodisiac taken in beer consumed at a brothel. Unfortunately there has so far been no opportunity for making further inquiries concerning the nature of the suspected "dope."

Between them these two cases present an interesting study of the symptoms produced by irritation of the urinary tract from renal pelvis to anterior urethra, and it is regretted that, owing to the difficulties of practising medicine on board a destroyer, it was not possible to investigate them in further detail.

G. A. BALLANCE, M.B., B.Chir.,
Surg. Lieut., R.N.V.R.

Influenzal Meningitis in a Child aged 2 treated with Sulphapyridine: Recovery

The following case is of interest as an example of the successful treatment of influenzal meningitis with sulphapyridine. A similar case has recently been reported by Birch in a child aged 3.

CASE HISTORY

The patient, a boy aged 2, was admitted to hospital on Dec. 11, 1942, with a week's history of a running nose and general malaise. Two days before admission he had a convulsion and became drowsy, and this was followed in a few hours by the onset of diarrhoea and vomiting, with constant twitching and rolling of the eyes. He had a past history of recurrent otitis media of the right ear, and measles five weeks before admission. He was the youngest of a family of four, the others being healthy.

When first seen he had a temperature of 100.4° and was drowsy and confused, with marked neck stiffness and a positive Kernig's sign. The right ear-drum was pink and opaque; the left one was normal. Lumbar puncture was performed, and the cerebrospinal fluid on the second day of illness was turbid and under increased pressure. It contained 2,740 cells per c.mm.—85% polymorphs—protein 190 mg. per 100 c.cm., and chlorides 755 mg. per 100 c.cm.; sugar was present. Sulphapyridine was started, with an initial dose of 1 g. followed by 0.5 g. four-hourly. The following day the child was still vomiting, and an intravenous infusion of 5% glucose in normal saline was given. He was very restless, and the temperature was still raised, but the right drum was no longer injected. The C.S.F. had grown a pure culture of a Gram-negative haemophilic organism, subsequently identified as *H. influenzae* on its requirement of both X and V factors. On the third day the child was very much improved; the temperature had fallen, and the saline infusion was stopped. Sulphapyridine was given in a reduced dose for a further five days, making eight days in all and a total of 17 g. On the tenth day the C.S.F. was sterile, and contained only 35 cells per c.mm., of which 80% were lymphocytes.

The temperature continued to fluctuate between 97° and 100° for three weeks, but the child was apparently well and had no physical signs. He was discharged on January 15, 1943, when he had been afebrile for a fortnight.

MARGARET E. MATTHEWS, M.B., B.S.,
R.M.O., Base Hospital, Hemel Hempstead (Great Ormond Street).

Reviews

WAR SURGERY

The Principles and Practice of War Surgery. With Special Reference to the Biological Method of Treatment of Wounds and Fractures. By J. Trueta, M.D. (Pp. 391; illustrated. 42s.) London: Hamish Hamilton Medical Books, in conjunction with William Heinemann. 1943.

Osler was wont to remind us that by the historical method alone can many problems in medicine be approached profitably, and the author of this book has made full use of such an approach to the problems relating to the treatment of war wounds. Through the practice of the great master surgeons of the past he traces for us how "the right philosophical basis produced the right technique."

The subtitle to the book is a happy one because its author's methods of treatment, by assisting natural repair as they do, may well be described as biological in character. How often in the past have misdirected surgical efforts retarded rather than assisted recovery! Dr. Trueta traces the surgery of war wounds from earliest times, from the days of early amputation of compound fractures to the beginning of the period of conservatism initiated by James Syme and William Fergusson, who in 1842 wrote: "It is a grand thing when by prescience even the tip of a finger can be saved." The author pays due tribute to his predecessors, including Winnett Orr, who instituted the methods which he has developed and which are here set forth in detail. While remembering that Winnett Orr, and possibly others also, may have been the originators of these methods, we do well to bear in mind an observation of Sydney Smith's, that "it is not the man who first says a thing, but it is he who says it so long, so loudly and so clearly, that he compels men to hear him; it is to him that the credit belongs." This applies very forcibly to Dr. Trueta, who has so clamorously and emphatically propounded these methods of early wound excision, drainage, and plaster fixation which are now becoming so widely known and practised so effectively, and with such good results, that the amount of suffering and the mortality from complications of wounds inflicted in this war have already been considerably less than they were in those of the last and so-called Great War of 1914-18. In the Spanish War he taught us that first aid for wounds should be avoided wherever possible, that the first intervention should be the main intervention, and wounds should be dressed as little as possible. He here describes what he calls his "five-point programme," consisting of (1) prompt surgical treatment; (2) cleansing of the wound; (3) excision of the wound; (4) provision of drainage; and (5) immobilization in a plaster-of-Paris cast. The methods of putting into operation the steps of this programme are illustrated by photographs of patients undergoing treatment. This five-point programme, with the details of how it can be carried out, constitutes the second and perhaps chief part of the present monograph: the former part is concerned with the pathology of wounds and the treatment of the wounded patient; and here we find very valuable discussions of such questions as infection, gas gangrene, tetanus, and shock.

The book is admirably printed in clear type, with excellent illustrations, and contains a comprehensive bibliography, and if its price appears high its quality is surprising for wartime and would appear to merit it. We venture to prophesy that it will become a classic of which most surgeons will want to possess a first edition. It is, perhaps, the most important monograph the war has so far produced. Embodying those correct biological principles which, as its author tells us, have been upheld by those men "who, believing in the benevolence of a Divine purpose, regarded themselves as its humble instruments," it marks another important transition period in surgical practice.

PAEDIATRIC GYNAECOLOGY

Pediatric Gynecology. By Goodrich C. Schauffler, M.D. (Pp. 384. $5.00 or 27s. 6d.) Chicago: The Year Book Publishers, Inc.; London: H. K. Lewis and Co. 1942.

This is a most interesting book, but it is more: it is a most useful one which should have a wide appeal. The everyday problems of the child with vaginal discharge, enuresis, pubertal bleeding, and pyelitis are but a few which the harassed physician is apt to treat indifferently and ineffectively for want of adequate direction and encouragement. Eighteen years ago Schauffler was faced with his first case of gonococcal vaginitis in a child of 3. After searching the textbooks and the literature for help he realized that this was not easy to find. Through the years that followed he made a careful and detached study of the female in infancy, childhood, and adolescence. Sixteen years of wide experience provided an excellent background and ample material from which to write a book devoted entirely to paediatric gynaecology.

The book is a comprehensive one. It opens with a concise review of the psychological factors so important to the successful handling of these cases. The technique of examination is then discussed in some detail, with due emphasis on points of practical importance, and a careful and well-illustrated account is given of the anatomy of the external genitalia, the vagina, and the cervix. The subjects of masturbation, vaginitis, and foreign bodies in the vagina are well handled in these same chapters. A comprehensive study follows of the menarche and those disorders of adolescence such as menorrhagia, metrorrhagia, and dysmenorrhoea. Pelvic viscera and pelvic peritonitis are the subjects of a separate chapter. A few pages are devoted to the consideration of pre-operative preparation, general principles of operative technique, and post-operative care, and these are followed by two excellent chapters dealing with lesions of the urinary tract and the lower bowel. The book concludes with a helpful discussion of social service and medico-legal problems.

The author is to be congratulated on his pioneer work and on the book he has written. It will be an excellent guide to all who are interested in this most important aspect of medical practice.

BOOKLETS ON FIRST AID

Air Raid First Aid. By W. A. Ashford, with foreword by W. A. Muir, M.D., D.P.H. (Pp. 46. 1s. 6d.) London: Williams and Norgate. 1942.

Emergency Street First Aid for Air-Raid Casualties. By Rufus Harris, M.R.C.S., L.R.C.P., First Aid Commandant, Exeter City Casualties Service. (Pp. 51.) Exeter: A. Wheaton and Co.

Of the making of "first-aid" books and booklets there appears to be no end. Each one has its merits, but each has its demerits. Notices of two which appeared in the first half of 1942 are given here.

Air Raid First Aid, by W. A. Ashford, is convenient for the pocket, written by a non-medical man, and commended by a medical officer of health. Its object is to present details of "reduced" treatment to be carried out at an incident. Taken as a whole it is clear, concise, dogmatic, and full of excellent suggestions and practical points. The question of "priority" in the treatment of casualties at a bombed site is answered well. It is perhaps a pity that "Bleeding, external," is separated from "Bleeding, internal," by a full chapter on wounds. By a few quotations it is not intended to disparage the contents but help towards improvement. Asphyxia in itself is not "want of fresh air"; it is the result of such a deprivation. Apropos of this a remarkable statement appears on page 45, amid some interesting "Odds and Ends." "Asphyxia. If you can't get a patient into the fresh air, take fresh air to the patient. A garden hose will do"! Fractures should be styled "closed" and "open," not "simple" and "compound." One thumb correctly applied in cases of arterial bleeding is sufficient; thumbs, or fingers, in the duplicate are not needed. The statement "Remember, a tourniquet is only required when a main artery is known to be severed," is not true; an artery may bleed furiously when only partially cut across. It is asserted on page 24 that the sympathetic nerves control the diaphragm and respiratory muscles, but neither anatomy nor physiology bears this out. A perusal of the booklet will repay the cost.

Emergency Street First Aid for Air-Raid Casualties, by Dr. Rufus Harris, has 51 pages and many diagrams. Not much perhaps new in this booklet, but the old clearly put. Some interesting details are given as to the correct position for a casualty on a stretcher. Attention is drawn to the fact that continued oozing of blood may lead to serious consequences if not discovered and dealt with. Good general rules for the first-aid treatment of fractures are given, but again the words "simple" and "compound" are wrongly used. In capitals on page 8 occur the words "GIVE NO STIMULANT" followed

by no idea as to whether this means "Give no alcohol" or "No stimulants are ever suitable to be given." Alcohol is not a "stimulant," but "hot tea" is. No remark is made as to the value of morphine in the relief of pain in burns and scalds. Taken with the extant textbooks this work forms a useful adjunct.

Notes on Books

The series "Britain in Pictures," in which *British Rebels and Reformers* appears, has won for itself a special position which this volume well maintains by its 8 beautiful colour plates and other drawings (William Collins; 4s. 6d.). As might be expected, the versatile Dr. HARRY ROBERTS is quite at home with his subject. He evidently believes with Jefferson that "a little rebellion now and then is a good thing." His good but necessarily rapid survey of the conditions which produced some of our national political and social rebels and reformers supports his statement that our history shows that it is love of justice rather than of riches, rather even than of liberty, that stirs the average Englishman to action. Dr. Roberts distinguishes between the rebel whose only weapon was revolt and the reformer who was able to use constitutional means of redress. Sympathetic as he is by temperament to the rebel, he does not fail to point out that responsibilities follow as a necessary consequence of power—a point that many of the rebels overlooked. He also shows that most of the rebellions and nearly all the reforms in this country have been backed by individuals who were not personally affected by the grievances they sought to remedy—Florence Nightingale and Lord Shaftesbury are good examples. There is nothing specifically medical in this book, but, as the author says, every Englishman should be interested in the things it deals with, for "politics, ultimately, is concerned, not with States and abstract policy, but with men and women who are born, see visions, fall in love and die"—a doctrine which is not without its implications in these days when "planning" is the fashionable cure-all and the individual runs a risk of being overlooked.

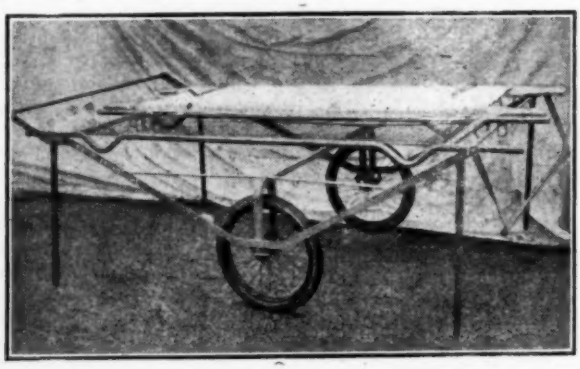
Preparations and Appliances

A WHEELED STRETCHER OR EQUIPMENT CARRIER

Dr. K. VERNON BAILEY, M.R.C.P., writes:

The stretcher carrier described below was primarily evolved to deal with Home Guard casualties and is based largely upon Home Guard needs, but it obviously would be of great value also for service with the Regular infantry and R.A.M.C. forces.

The main disadvantages of the hand-carried stretcher are: (1) its limitations over a long distance; frequent rests for the bearers become necessary and the slow and uneven progress detracts from the patient's prospects; (2) its extravagant demand on personnel; a heavy casualty may require four men to transport the loaded stretcher a matter of 300 yards, at the end of which time the bearers are temporarily exhausted. Moreover, in open contact with the enemy it is not always to be expected that casualty collecting points will be within convenient hand-carrying distance from forward positions; those that are may, during an engagement, either become



further removed by the advance of these positions or be put out of action altogether. Further, motorized ambulance transports may not be able always to approach directly to the position of forward collecting points to complete the evacuation. Too great a reliability is placed on their being able to do this in the organization of Home Guard defence and too little consideration given to the following facts: (1) the number of casualty collecting points is large (on a platoon basis); (2) their exact positions may be difficult to find; (3) the number of motor ambulances is limited; (4) motor ambulances themselves require either roads or a relatively smooth surface over which to travel; and (5) the forward area to a depth of a mile or more is under fire.

An area some one to three miles in depth behind the line of contact with the enemy is likely to be embarrassed in the matter of communication, congested so far as road traffic is concerned, and continually subjected to the effects of the action in progress. Under these conditions it is essential that casualties of the first priority should be evacuated immediately to a position of relative safety, where they can receive adequate temporary treatment, or from which they can be transported to a hospital or clearing station. The best method of doing this is to use a special hand-propelled wheeled stretcher carrier. The most efficient and economical type of such carrier is one which is light to handle, easy to transport when unloaded, strong enough to take the weight of two loaded stretchers, and can be loaded and propelled by two bearers.

Suggested Design for Metal Carrier

A light carrier has been made to this design by Lieut.-Col. Crooke, commanding 49 Lancs H.G. The technical description is as follows. The framework is so constructed of metal sections that it is flexible in itself; it is mounted on 8 coil springs, each supporting a load of 50 lb., transferring the load to the road wheels fitted with 20 in. by 2 in. by 1¾ in. pneumatic tyres which can be inflated by a cycle pump. There is a fixed handle-bar at one end for control, and a folding handle-bar at the other end for traction. Four supports are provided, one at each corner held in a folded position with a link and readily manipulated. The axle is arranged to give the maximum ground clearance. The wheels can be removed in the same manner as a cycle wheel. The general service and civil defence stretchers can be used. The carrier is painted with anti-gas paint and weighs 100 lb.

The springing minimizes all jolts or jarring during transport, and the carrier can be dismantled for transportation by simply dropping it out of the wheels, which are packed separately. It is quickly and simply loaded by placing the stretcher on the two transverse cross-bars, which fit accurately against their runners, and it is easily controlled by two men. The corner stands are quickly released to steady the carrier for loading or in an emergency, and are rapidly secured again in place. It is important to place the stretchers with the heads of the patients at the pulling-end of the carrier; this has the effect of weighing down the pulling-end and thus enabling the bearer at the pushing-end to lean on the bar and so exert easy pressure. The carrier loaded with two stretchers, each bearing a patient weighing approximately 11½ st., plus their full equipment, including great-coats, blankets, etc., was transported over a distance of two miles (mostly uphill and including a 200-yard hill of 1 in 6 gradient) in under 30 minutes without undue hurry, exertion, or fatigue. Barriers which could not be surmounted by a motor ambulance were negotiated by unloading the carrier, transporting the loaded stretchers and carrier separately by hand, and reloading on the other side.

CENTRIFUGE TUBE FOR COLLECTION OF LEUCOCYTES

Dr. M. A. GOHAR, Ph.D., M.R.C.P., writes from the Faculty of Medicine, Cairo:

For the preparation of a leucocyte suspension, one of the usual procedures is to centrifuge citrated blood in an ordinary centrifuge tube and to collect the greyish layer that floats on the surface of the red blood corpuscles. This, however, is not always easy since the film is so thin that, when taken, one usually finds that the great majority of the cells are red blood corpuscles and that the leucocytes are rather scanty. The cause of this difficulty is that the film collects on a big surface. If this area could be made smaller, the thickness of the film

ONE-THIRD SCALE

would obviously be increased and the leucocytes would therefore be much easier to collect. This led me to suggest the use of a centrifuge tube having the shape illustrated in the figure. It is needless to say that it should be made from the strong glass from which centrifuge tubes are usually made. It has actually been made locally to my satisfaction in the glass factory of Messrs. Sayed Yasin and Co., Cairo.

The tube is filled with citrated blood up to the mark A and centrifuged. The upper level of the corpuscles falls in the narrower part of the tube. Since the surface area here is small the film of leucocytes on the top of the red blood corpuscles is relatively thick and is easier to collect than a film in a wide ordinary centrifuge tube with a wide surface area.

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MEDICAL APPLICATIONS OF THE CYCLOTRON

Popular interest in the cyclotron has been stimulated by its description as an "atom-smasher," but a more accurate name for its effects would be "nuclear transformation."[1] With the discovery of radio-activity the existence of natural transmutation of atoms was demonstrated, and the first artificial transmutation (of nitrogen into oxygen) performed by Rutherford in 1919 directed attention to the means of energizing particles to such a degree as would enable them to penetrate the nuclear barrier. While the methods of attaining very high voltages in order to give a particle high energy by a single big push made steady progress, J. H. Lawrence experimented with the idea of using much lower voltages tuned to give the particle a series of pushes. Thus the cyclotron emerged—an apparatus in which the particle is kept moving in a circular path by a magnetic field and intermittently accelerated by an electrical field. The particles move inside two hollow semicircular electrodes placed between the poles of an electromagnet, and are accelerated by an oscillating potential applied to the electrodes every time they cross the central gap between them. The angular velocity of the particle produced by the magnetic field is constant, but the successive accelerations of its linear velocity produced by the electrical field cause it to move in an ever-widening flat spiral. Its ultimate energy is thus limited only by the diameter of the hollow electrodes. Lawrence's early model was 11 in. in diameter, and produced protons with an energy of 1.25 million electron-volts (mev.). Then came a 27-in. cyclotron with an 80-ton magnet, subsequently increased to 37 in., and giving particles with 8 mev. energy. The discovery of the neutron by Chadwick in 1932 and the isolation of heavy hydrogen by Urey in the same year greatly facilitated atomic transformations, for, whereas the proton $_1H^1$ has to overcome the repulsion exerted by the positively charged nucleus of the atom, the neutron of the deuteron particle $_1H^2$ meets with no such opposition. (The superscription refers to the mass of the atom and the subscription to its charge: thus the deuteron $_1H^2$ has a mass of 2 and a single positive charge.)

Atomic transformations result in excited atoms which emit energy in various forms—that is, artificial radio-activity is produced. For example, a proton captured by a lithium nucleus results in an unstable beryllium nucleus, which splits into two α-particles (or helium nuclei) with an energy of 8.5 mev.: $_1H^1 + {}_3Li^7 \rightarrow {}_4Be^8 \rightarrow 2_2He^4$. The neutron of a high-speed deuteron may be captured by a phosphorus nucleus, and the radio-active phosphorus then emits a β-particle (or electron) with 1.7 mev. energy and becomes sulphur: $_1H^2 + {}_{15}P^{31} \rightarrow {}_1H^1 + {}_{15}P^{32} \rightarrow {}_{16}S^{32} + {}_{-1}e^0$. Or the whole deuteron may enter a beryllium nucleus, yielding a very unstable boron nucleus, which at once emits a neutron of very high energy, 21 mev.: $_1H^2 + {}_4Be^9 \rightarrow {}_5B^{11} \rightarrow {}_5B^{10} + {}_0n^1$. Thirteen types of nuclear reaction have been observed, and radio-active isotopes of every known element have been produced. With the 37-in. cyclotron, however, the yields of artificially radio-active elements were small, and in 1939 a 60-in. cyclotron with a 200-ton magnet was completed specifically for medical application. Producing particles with 16 mev. energy, its yield of radio-active elements is some five times that of the 37-in. cyclotron. A giant 184-in. is now nearing completion, with a magnet weighing 4,000 tons; it will produce deuterons with an energy of 100 mev., giving thirty-five times the yield of radio-active substances from the 60-in. "medical" cyclotron. But more than a greatly increased yield is expected from this giant cyclotron: the energy of its particles will approximate to that observed in cosmic ray phenomena, so that new atomic processes are likely to happen. When mass disappears, energy appears in its place: according to Einstein's theory, the energy released is equal to the mass multiplied by the square of the velocity of light—i.e., 9×10^{20}—and this relationship has been verified for the proton–lithium reaction producing two high-speed α-particles. The hundred-million-volt cyclotron will certainly be used for investigating the possibilities of atomic power.

The three major fields of biological study developed about the cyclotron have been surveyed by Hodges,[2] and formed the subject of a symposium at a meeting of the Radiological Society of North America.[3] First, there is the use of a radio-active element to trace the absorption, utilization, and excretion of its stable isotope by the body in both health and disease.[4] Secondly, there is the therapeutic effect of the radiations emitted by radio-active substances internally administered. Thirdly, beams of both fast and slow neutrons are being used in the treatment of cancer in a manner similar to x rays and γ rays in external radiation therapy.[5] Metabolic studies by the classical methods of chemistry and physics need relatively large quantities of the elements to be investigated; these disturb the normal balance of such elements in the body, and the methods employed cannot differentiate between what has been administered and what was already in the body. The radio-active tracer substance reveals the metabolism of an element with a sensitivity several million times greater than that shown by chemical methods, by the measurement of the radio-activity of organs and tissues either *in situ* or in samples of tissues after removal from the body. In the latter case, also, an autoradiograph of a thin slice of tissue can be directly compared with the stained histological preparation. For example,[6] this method has shown that iodine is taken up in larger amounts by hyperplastic thyroid cells than by the normal cells, but that it is not taken up at all by cancerous thyroid cells. Thus, while radio-active iodine may be of value in the treatment of thyrotoxicosis, it is unlikely to help in the destruction of malignant disease of the thyroid. The rapidity of the metabolic processes of the body is well illustrated by the fact that within four hours of administration over nine-tenths of the radio-active iodine has been combined into the organic compounds thyroxine and di-iodotyrosine. Incidental to the researches on iodine metabolism, the missing element 85, belonging to the halogen series and not yet found in Nature, has been artificially produced and found to be radio-active. Its halogen nature was confirmed by its selective absorption by the thyroid gland, though to an extent only about one-third of that of iodine.

Only weak activities of radio-active calcium have been available, but radio-active strontium can be readily prepared in large amounts and emits energetic β rays, and has the useful half-life period of 55 days. It is selectively deposited in actively growing bone, including bone tumours, so that

1 Aebersold, P. C., *Radiology*, 1942, **39**, 513.

2 *Radiology*, 1942, **39**, 440.
3 Ibid., p. 513.
4 *British Medical Journal*, 1941, **1**, 368; **2**, 733.
5 Ibid., 1941, **1**, 447; 1943, **1**, 481.
6 Hamilton, J. G., *Radiology*, 1942, **39**, 541.

it is likely to have therapeutic applications in adults suffering from osteogenic sarcoma; the possibility of destroying early pulmonary metastases at once presents itself. The use of radio-active carbon has upset two accepted theories—of the photosynthesis of carbohydrates by green plants and of the manufacture of glycogen in the liver from lactic acid. Ruben and Kamen[7] have shown that the initial reaction involving each assimilated carbon dioxide molecule is its reduction to a carboxylic acid group, and that this is a non-photochemical reaction. Hastings administered lactic acid containing radio-active carbon atoms, but none of these labelled carbon atoms could be detected in the liver glycogen; when sodium carbonate was used as the vehicle for the radio-active carbon, all the labelled carbon was recovered from subsequently elaborated glycogen. These examples are sufficient to illustrate Hamilton's conclusion that, while the classical procedures of chemistry and physics yield a static picture of biochemical processes, the radio-active tracers reveal the dynamic pattern of the chemical integrations taking place in the living cell.

Some instances of the practical application of this new physical knowledge have already been given. Naturally the possibility of applying radiation selectively to malignant cells is one that has aroused the most intense interest. Radio-active phosphorus is selectively accumulated in the nuclei of rapidly multiplying cells, and the results of its therapeutic use in 222 patients with leukaemia and allied diseases are reported by Low-Beer, Lawrence, and Stone.[8] Trials of different methods of dosage suggest that the best results follow intravenous injection of small weekly doses sufficient to maintain a radio-active level of from 3 to 8 millicuries. The clinical results in polycythaemia vera and multiple myeloma are much better than from any other known treatment; in leukaemia they are at least as good as from *x*-ray therapy; but in Hodgkin's disease they are disappointing—a combination of deep *x*-ray therapy and radio-active phosphorus is now being tried. The results in 22 cases of lymphosarcoma reported by Kenney and Craver are also rather disappointing, in that the response of the disease to radio-active phosphorus ran parallel to that to *x*-ray therapy, so that where *x* rays had failed to control the disease P^{32} also failed. A valuable report by Stone and Larkin[9] on radiotherapy by fast neutrons establishes the degree of dermal, mucosal, and general reactions to be expected from given doses. Curative results were not anticipated, as the 120 patients so far treated were chosen because of their unsuitability for treatment by surgery, radium, or *x* rays. The neutron beam was produced in the 60-in. cyclotron by the bombardment of a beryllium target with 16 mev. deuterons, giving neutrons with energies up to 21 mev. and γ rays; after passage through 3 cm. Pb the beam comprises 95% neutrons and 5% γ rays. There is no significant scatter, so that the "air-dose" and the "skin-dose" are the same; the depth dose at 10 cm. for a 10×10 cm. field is 40% of the surface dose. At the end of treatment about 17% of the patients showed complete regression and 48% partial regression of the tumour; perhaps the most encouraging observation was that epitheliomatous metastases in the lymph glands of the neck responded better than the primary tumour; while on the debit side was the persistence of ulceration at the site of the primary tumour, even though biopsy from the margin of the ulcer showed no evidence of cancer. It looks as if the intensity of ionization in the tissues is such as to destroy impartially both the cancer cells and the stroma, but different combinations of the dose, time, and intensity factors will require trial before the place of fast neutrons in the radiotherapy of cancer can be assessed.

[7] *J. Amer. chem. Soc.*, 1940, **62**, 3443.
[8] *Radiology*, 1942, **39**, 573.
[9] Ibid., p. 608.

THE CAUSE OF MYASTHENIA GRAVIS

Recent advances in physiological knowledge have seldom been applied to the study of disease so readily as in the case of the chemical factors subserving transmission of nervous impulse at the myoneural junction. As each step in knowledge in this field has been made it has been applied to diseases thought to be caused by disorders at the myoneural junction, of which myasthenia gravis is the outstanding example. In an orderly series of papers from the Johns Hopkins Hospital[1 2 3 4] Harvey and his colleagues have continued to study the mechanism of the transmission of impulse from nerve to muscle in man by the investigation of normal and abnormal subjects. They point out that the evidence that the disorder in myasthenia gravis is at the myoneural junction is overwhelming, and postulate three possible forms which this abnormality may assume. First, there may be an excessive concentration of cholinesterase, which by hydrolysing the released acetylcholine prevents the sustained transmission of nervous impulse and consequently muscular contraction. Secondly, the excitatory threshold of the muscle end-plate to the normal quantity of acetylcholine released by each nerve impulse reaching the neuromuscular junction might be raised. Thirdly, each impulse reaching the neuromuscular junction might fail to release a normal amount of the transmitting agent, causing in effect a physiological denervation. Harvey and his co-workers show that, whereas in normals intra-arterial injection of prostigmine caused a diminution of the contraction of striped muscle, it causes an increase in myasthenic subjects. When a retaining cuff is released the effect spreads from the muscles nourished by the artery to muscles elsewhere in the body. When acetylcholine is injected into an artery of a normal subject who has received prostigmine previously, there are flushing and sweating of the distal extremity, with immediate deep pain and weakness of muscles, followed by fibrillation. This, as they explain earlier, is due to the paralysing effect of too great a concentration of acetylcholine at the junction, made possible in normal people by the presence of prostigmine, which inhibits the destruction of the acetylcholine by the cholinesterase normally in the blood stream. In myasthenics, on the other hand, although flushing, sweating, and pain are present as in normal persons, violent muscular contractions, going on to spasm similar to the carpopedal spasm of tetany, occur in place of the muscular weakness seen in normal subjects. These contractions are much more powerful than would be possible with purely voluntary contraction of the muscles. In the myasthenic, also, the rapid, flickering asynchronous fasciculations which they observed in the normal subjects were not encountered.

The authors proceed to list the many points of resemblance between myasthenia gravis and partial curarization, but they go on to show that, whereas the myasthenic muscle is exquisitely sensitive to acetylcholine, the partly curarized muscle is much less sensitive to it than is normal muscle. The great sensitivity of completely denervated muscle to injected acetylcholine is well known,[5] and the similarity between the physiological behaviour of denervated and of myasthenic muscle when exposed to the substances modifying transmission at the myoneural junction is close. Harvey and his colleagues conclude that the evidence they present supports the view that in myasthenia gravis there is a reduction in the amount of acetylcholine released at the junction. This may be due to one of three things: first, a reduction in the store of the transmitter or its precursor; secondly, unusual susceptibility to abnormally

[1] *Johns Hopk. Hosp. Bull.*, 1941, **69**, 1.
[2] Ibid., p. 529.
[3] Ibid., p. 547.
[4] Ibid., p. 566.
[5] *Amer. J. med. Sci.*, 1939, **198**, 737.

rapid destruction ; and, thirdly, a normal store of transmitting substance which, although available, might be blocked in its action by another substance. They present evidence in support of the third possibility.

As myasthenia gravis is characterized by the occurrence of spontaneous remissions and the defect in transmission is temporarily repaired by other substances, the reversible character of the disorder is emphasized. From the mass of evidence they produce it seems reasonable to assume on physiological grounds that some independent inhibitor substance released into the circulation in varying amounts might be responsible for the functional defect which is found. Gammon, Harvey, and Masland[6] have shown that this hypothetical substance might well be derived from the thymus gland. Abnormality of the thymus is found at necropsy in a very large proportion of myasthenics, and the results of surgical thymectomy in severe myasthenics, carried out in this country by Keynes,[7] have in some cases been brilliant. The whole story is not yet known, and the more acute and severe myasthenics, with generalized weakness, seem to benefit most by operative removal of the thymus. Those with weakness confined to muscles having a bulbar innervation do not respond so well as those with weakness of spinal muscles. Nevertheless it is encouraging to find the results of physiological research being translated into therapeutic achievement even if the full effects of surgical intervention are not yet understood.

POLIOMYELITIS VIRUS IN WATER

Poliomyelitis virus has been demonstrated in the faeces of persons suffering from the disease and has been shown to persist for a long time in sewage. The gastro-intestinal tract is now recognized as a portal of entry for the virus, so that drinking-water contaminated secondarily from sewage must be looked upon as a potential source of infection, though no case has, as yet, been traced directly to such water. Poliomyelitis virus is known to persist for 100 days and more in sterile water stored in the dark, and modern methods of chlorination leave it unaffected. Carlson, Ridenour, and McKhann[8] have lately investigated whether the water-purification methods in common use will remove the virus from artificially infected water. They used a neurotropic virus pathogenic to mice—apparently an adapted poliomyelitis strain. Coagulation and sedimentation procedures with lime and alum caused but a slight reduction of the amount of virus in suspension, and this reduction was roughly proportional to the amount of virus present. During these experiments it was noted that this neurotropic virus withstood a *p*H range of 3.5 to 8.0. Sand filtration was carried out in the laboratory in a model filter with constant head of water. The virus was not held back by sand filtration alone, but when large quantities of alum floc were allowed to impregnate the surface layers of the sand filter, with consequent diminution of filter flow, only one mouse of 54 inoculated with the filtered water developed paralysis, while control groups of mice were paralysed, showing the virus to be present and active in the supernatant water. It was found that a large accumulation of floc was required to hold back the virus, because, in a later experiment, a measured layer of floc of 1/8 in. thickness did not restrain it. Partial adsorption of the virus on activated charcoal was demonstrated in concentrations of 10, 25, and 50 parts per million in water. Injection of the charcoal into mice showed the virus to be concentrated on the particles. Suspensions stored in tap water in the refrigerator remained viable for more than a hundred days, and aeration had little apparent effect on the virus. Irradiation with ultra-violet light effected a big reduction of virus suspension in water. Of the 36 mice used in the irradiation experiments only 3 became paralysed and died, while all but 1 of the control group of 18 animals which received a 1 in 300 dilution of untreated virus became paralysed. Direct sunlight did not destroy the virus as effectively as did ultra-violet light, which was, in fact, the most effective of all the water-purification methods investigated.

6 *Biol. Symp.*, 1941, **3**, 291.
7 *Proc. roy Soc. Med.*, 1943 (in press).
8 *Amer. J. publ. Hlth.*, 1942, **32**, 1256.

CASTRATION FOR PROSTATIC CARCINOMA

In the spring of 1941 Huggins and his co-workers reported a series of cases of carcinoma of the prostate which had been treated either by castration or by the administration of oestrogen, or by both methods combined. The results were unexpectedly favourable, even when extensive bony metastases existed. Huggins assessed his results chiefly by clinical data but also by the fall of acid phosphatase, which is usually much increased in cases of prostatic carcinoma. Since the publication of his paper this form of treatment has been adopted by many other surgeons. R. Chute and A. T. Willetts have recently reported[1] on thirty-seven cases treated by these means. Only one patient would appear to have received no benefit. Beneficial results included rapid, effective, and lasting relief from the pain of metastases, increase in weight, and improvement in appetite, strength, and general well-being. Nine out of 13 cases with retention were able to pass urine after treatment by orchidectomy and stilboestrol. Determination of the acid phosphatase showed that when its level was above normal it fell rapidly after castration, and still further with the giving of stilboestrol. No dangerous or harmful effects were noted, though, as was to be expected, libido and power of erection disappeared in most cases. The results of stilboestrol therapy were in every way as good as those obtained by castration, but since the effect of stilboestrol lasted only while it was being given, the favourable action obtained from castration was more permanent. For this reason alone it has a considerable advantage. Quite naturally some patients dislike the idea of such an operation, and the technique suggested by L. W. Riba[2] avoids some of the psychological disadvantages inherent in castration. The operation is performed as follows : The anterior scrotal wall is infiltrated with 1% novocain and 10 c.cm. of the anaesthetic injected directly into each spermatic cord. The testicle is then delivered through a 4 or 5 cm. incision and the anterior surface of the tunica vaginalis and albuginea incised. The exposed parenchyma can easily be removed through this incision by blunt dissection. Bleeding is easily controlled by ligature, and when haemostasis has been secured the incised capsule of the testicle is sutured. Both testicles can be treated through the same median scrotal incision. As a rule the patient is unaware of their absence.

RIBOFLAVIN AND CORNEAL VASCULARIZATION

The syndrome of ariboflavinosis, or riboflavin deficiency, was first described in 1938 by Sebrell and Butler,[3] who recorded the angular stomatitis, reddening, fissuring, and desquamation of the lips, and the seborrhoeic lesions of the nose, eyelids, and ears that occur in this syndrome. In 1940 Kruse and his colleagues[4 5] added to these appearances a frequently fissured magenta-coloured tongue with

1 *New Engl. J. Med.*, 1942, **227**, 863.
2 *J. Urol.*, 1942, **48**, 384.
3 *Publ. Hlth. Rep.*, Wash., 1938, **53**, 2282; 1939, **54**, 2121.
4 Ibid., 1940, **55**, 157.
5 *J. Amer. med. Ass.*, 1940, **114**, 2437.

flattened papillae, and for the first time also described certain ocular lesions characteristic of ariboflavinosis—roughness of the eyelids, photophobia, inability to see in a dim light, lacrimation, impairment of visual acuity, keratitis, and corneal vascularization. They stated that the earliest and most common sign of ariboflavinosis is circumcorneal injection, which if not grossly visible is seen on slit-lamp examination. Since 1940 corneal vascularization has come to be regarded as a certain diagnostic sign of ariboflavinosis, and American nutrition surveys[6] have used it as an index of riboflavin nutrition. Recently, however, the value of this sign has been questioned in both this country and America. In an article in this *Journal* Scarborough[7] recorded an incidence of circumcorneal injection of 34% in a series of 204 unselected out-patients in Edinburgh (68% in patients over 50), and Sandstead[8] has found the condition extremely common in school children and young adults in America, the incidence ranging from 80 to 93% in the various groups studied. In Sandstead's cases riboflavin in doses of 5 mg. daily caused no significant change in the degree of corneal vascularization. Scarborough made a similar observation. At present, therefore, corneal vascularization is a doubtful diagnostic sign of riboflavin deficiency unless supported by other clinical findings such as angular stomatitis, reddening and desquamation of the lips, ocular symptoms, and the seborrhoeic dermatosis of the face.

The supposed association between rosacea keratitis and ariboflavinosis has also been challenged. In 1940 Eckhardt and Johnson[9] suggested that rosacea keratitis resulted from riboflavin deficiency because of the improvement after administration of riboflavin and because of the possibility that the telangiectasia and corneal vascularization of rosacea keratitis might be physiological responses of the blood vessels to deficient oxidation resulting from the failure of the flavo-protein enzyme system, of which riboflavin is a component. These authors claimed to have cured cases of rosacea keratitis with injections of 1 to 2 mg. of riboflavin. Recently Fish[10] has been unable to verify this claim. In 40 out of 45 cases of rosacea keratitis she was unable to find the type of vascularization described by the American authors as characteristic of ariboflavinosis. Treatment with riboflavin alone was unsuccessful; many of the patients actually became worse owing to the withdrawal of atropine. The lesions of controls healed under routine treatment. It has now been established that the concentration of riboflavin in the corneal epithelium of the ox is very high, and it may be that in patients already suffering from ariboflavinosis and with corneal lesions the administration of the vitamin may promote healing; this might explain its beneficial action in the cases described by Eckhardt and Johnson.

RETINAL VENOUS CHANGES IN DIABETES

Ophthalmoscopic findings in cardiovascular lesions have the great drawback that they are but poorly elucidated by histological studies, for these are exceptional. It is one of the merits of the Mackenzie Memorial Lecture by Prof. A. J. Ballantyne[11] that the wealth of clinical detail he reports is substantiated by pathological studies. Of necessity there is much that is conjectural in his discussion of changes in the lumen of vessels, comprising, among others, such an entity as transitory spastic contraction. His insistence on checking appearances by established pathological data does, however, give validity to his discussion where no such evidence is available. Thus he is able to remind us that a retinal artery which looks white to the ophthalmoscope is not necessarily an obliterated artery, for qualitative changes in the vessel wall as well as obliteration of the lumen can give this effect. His critical survey of our knowledge of these and allied appearances, such as those seen at the arteriovenous crossings, lends point to his personal observations. He rightly states that, while much attention has been given to changes in the arteries, relatively little has been allowed to changes in the veins; yet, as he shows, the veins, too, can undergo spasm. But what is particularly significant is the series of changes in retinal veins that he ascribes with a high degree of probability as pathognomonic of diabetes. The picture, as he presents it, is characteristic enough. There is irregular beading of a gross type in the larger veins, tending to produce loops which, histologically, he has found to be pre-retinal as well as retinal. The obvious interference in venous flow shows itself in secondary retinal changes. Gross venous obstruction, such as is seen in thrombosis of the central vein, is not a feature. The attention he focuses on the veins in diabetes may help to explain some of the characteristic vascular lesions the clinician recognizes as diabetic without being able to distinguish them clearly from somewhat similar changes in simple retinal arteriosclerosis.

HIPPURIC ACID SYNTHESIS AND LIVER FUNCTION

The hippuric acid test of liver function—based upon the excretion of hippuric acid in the urine after ingestion of sodium benzoate—is noticeably less popular here than in the United States, where it was introduced by Quick.[1] This may be due to its theoretical disadvantages, such as the uncertain influence on the result of rates of absorption and excretion. The former may be obviated by giving the sodium benzoate intravenously,[2] but renal damage must always be considered and may partly account for the impaired excretion found in obstructive jaundice and after surgical operations.[3] Nevertheless there are many cases in which the kidneys can be trusted to play their part satisfactorily, and the relative convenience of the test is a strong point in its favour. A recent report by Rennie[4] from Glasgow is therefore of special interest. Using the oral technique, he found low excretion in 13 out of 17 cases of infective hepatitis, in 5 out of 5 cases of acute toxic hepatitis, in 12 out of 14 cases of hepatic carcinomatosis, in 13 out of 14 cases of cirrhosis, in 8 out of 10 cases of obstructive jaundice, and in 4 out of 24 cases of cholecystitis. This leaves little doubt that the test is a sensitive indicator of hepatic damage, but raises the question of the way in which it is likely to be clinically useful. It is evident that the diagnostic possibilities are limited, similar results being obtained in all types of liver disease, including obstructive jaundice. It may evidently be useful in revealing latent liver damage—e.g., in hyperthyroidism[5]—in studying the impaired function in known hepatic diseases, and in assessing recovery from toxic and infective hepatitis.[4] The test has been used prognostically by Boyce[3] in obstructive jaundice and in various surgical conditions, and the statement has been made by Delor and Reinhart[6] that patients excreting less than 2 grammes are usually a poor operative risk. This important claim merits further investigation in view of the possibility of improving liver function in these cases by suitable pre-operative therapy.

6 *Publ. Hlth. Rep.*, Wash., 1942, **57**, 189.
7 *British Medical Journal*, 1942, **2**, 601.
8 *Publ. Hlth. Rep.*, Wash., 1942, **57**, 1821.
9 *Arch. Ophthal.*, Chicago, 1940, **23**, 899.
10 *Brit. J. Ophthal.*, 1943, **27**, 107.
11 *Glasgow med. J.*, 1942, **138**, 1, 52.

1 *Amer. J. med. Sci.*, 1933, **185**, 630.
2 *Amer. J. dises. Dis.*, 1939, **6**, 716.
3 *The Role of the Liver in Surgery*, Springfield, Ill., 1940.
4 *Brit. J. exp. Path.*, 1942, **23**, 329.
5 Haines *et al.*, *Ann. intern. Med.*, 1941, **14**, 1225.
6 *Amer. J. clin. Path.*, 1940, **10**, 617.

SOME OBSERVATIONS RELATING TO THE PLANNING OF MEDICAL EDUCATION

BY

FRANCIS DAVIES, M.D., D.Sc.

Department of Anatomy, University of Sheffield

In recent years much has been written, and a great deal of disquiet expressed, concerning the present status and the future planning of medical education. Various committees are to-day considering the general changes in medical education which appear to them to be necessary, and universities and medical schools throughout the country have been invited to report their views on these problems to the Interdepartmental Committee on Medical Schools of the Ministry of Health. It may be observed that one body which is taking upon itself the onus of investigating these matters plays no part at all in the actual teaching of the medical student. The time seems ripe for a frank statement on considerations which do not appear in the foreground of previous writings on these problems, but which should receive careful attention in the present deliberations. They comprise, first, the quality of the prospective entrant to the medical profession, and, secondly, the adverse influence which the existing examination system (at least in some subjects) has upon the "education" of the medical student.

The Curriculum

Some rigidly separate medical education into two sections—namely, scientific education and vocational instruction—and lay emphasis on the necessity for paying particular attention to the latter at the expense of almost complete elimination of the former, on the ground that we are instructing students the great majority of whom are destined to become general medical practitioners. The implication may be drawn that the curriculum should be so fashioned that the bare minimum must be taught in order that the type of student with whom we have to deal can safely and relatively easily cope with it. Now, it must be the opinion of every teacher of some years' experience that the better students take the present curriculum in their stride; they are even avid for more information, over and above that given to their contemporary classmates in the formal lectures and practical classes, and, by a stimulating and progressive teacher, they are readily encouraged to read widely around the narrow confines of the formal classes they attend. On the other hand, it is sadly true that too high a proportion of our medical students are not up to the standard which should be required of a person who is to be entrusted with matters relating to the health of the community. These students just manage to crawl along the curriculum, failing the examinations sprinkled through the course time after time, till eventually, after descent in many cases from degree to diploma courses, they scrape through a final qualifying examination. A relatively long tail of such students is found, particularly in schools catering for large numbers, where nothing approaching individual attention is attained. Most of these students succeed in passing the several examinations after two or more attempts at each, and, even when they eventually pass, they just manage to obtain one or two marks over the minimum pass-mark.

This state of affairs must certainly be considered unsatisfactory. It is surely not the desire of those responsible for remodelling the curriculum to bring down the standard or scope of the various subjects to the level of such students. We must face the fact, known to university teachers in the pre-clinical years, that their colleagues in the other faculties of the university are of the opinion that many students in the Faculty of Medicine are not of the best quality, and, indeed, some of these teachers who deal with medical students in the first year of their course are not unwilling to state that many medical students are not of the standard of the majority of those taking university courses in other faculties. Furthermore, relevant to the present discussion, it must be a common experience for teachers in the Medical Faculty to learn from some of their colleagues in other faculties (many of whom have attained eminence in their particular subject) that they themselves would have liked to enter the medical profession in their earlier years, but were precluded from doing so by financial considerations.

The Prospective Medical Student

It appears to me that a radical alteration which is urgently needed is to eliminate financial obstacles and thereby place ourselves in the position of being able to choose the best talents among prospective students from all walks of life. As a corollary to this, the weakling should be ruthlessly eliminated *in the early years of the course*. By such means the quality of the "raw material" could be considerably improved and a high-standard curriculum evolved, the student being educated to this standard and not the standard degraded to the level of a second-rate student. The manner in which the financial obstacles may be overcome needs consideration; and, while undertaking this, it must be borne in mind that the present trend of economic developments (e.g., as outlined in the Beveridge report) will probably lead to the demand for a considerable increase in the number of doctors to qualify each year, entailing the calling for supplies of suitable students from a wider section of the population. The following suggestion is made with the appreciation that others may be formulated as more economically sound, although, so far as I can see, the general principle should be readily acceptable.

In the discussion by the General Medical Council (Winter Session, 1942) of the draft memorandum from the subcommittee appointed to prepare evidence for the departmental committee of the Board of Education, Sir Farquhar Buzzard expressed his opinion that one of the chief causes of early specialization (i.e., in the schools) was the scholarship and the competition between schools for this purpose. He urged that the scholarship should be awarded for merit and should bear no relation to the future career of the student. The choice of medicine could be made after the award, and in no other way would the right kind of medical student be selected. This observation was made in view of the fact that during the last year or two of his school career a student who was known *at that time* to be desirous of entering the medical profession was crammed in a small number of science subjects in order to sit for a university entrance scholarship examination. Thereby his general education was severely restricted; and it is literally true, for instance, that many medical students are not able to write a lucid, grammatically correct answer to a question, although the factual content of the answer may be reasonably accurate. This state of affairs may be largely eliminated by the following means.

The entrance scholarship in its present form should be discontinued. A broad general education of the student should be continued up to the time when application is made for his acceptance by the university as a medical student. The candidate for entry should be required to sit a university entrance examination, which should be set and assessed by the university, and which should be wide in its scope, involving a good general education and not a high standard of knowledge in one or two subjects only. The standard attained in this examination would be taken into account in considering (*a*) whether the boy was fit for entry, and (*b*) whether he should be awarded a "scholarship." (This question of entrance scholarships should be considered by the reader in conjunction with that of "post-entry scholarships," discussed below.) The boy's application for entry might be accompanied by a "recommendation" from his head master, this being based on the character, general standard, and development of the boy throughout his school career. This recommendation would be received, together with all the boy's detailed school reports (including examination assessments), by a university committee, whose personnel should comprise representatives of all faculties, and whose function it would be to determine whether the boy was of sufficient standard for entry, whether he appeared likely to benefit from a university education, and whether his predilections indicated his suitability for acceptance as a medical student. The boy would be interviewed by the committee, which in the above ways could satisfy itself that the candidate for entry had received a sound general education. (These procedures would apply with advantage to all prospective university students, irrespective of their preference for any particular branch of study in the university.)

The Financial Aspect

Let us suppose that such a candidate, having satisfied the full requirements for acceptance as a medical student, is found

to be unable to afford the expenses incidental to a medical education. The university committee would report to an appropriate Government Departmental Committee and the boy would be given State aid, the amount being determined by the financial status and commitments of the boy's parents, but, if necessary, the amount should be enough to cover completely the boy's expenses, including living expenses, fees, books, instruments, etc. Such aid being granted, the boy would undertake to repay the "loan" (free of interest) when he begins to earn his living, by means of a percentage (say, 5%) of his *net* annual earnings. Even if he has to repay all the money expended by the State on his behalf it would not be an unduly heavy burden for him to bear. (We must remember in this connexion that were it not for this State aid he would not have been able to enter the medical profession at all.) But the boy should be given opportunities of reducing the amount repayable, by means of "scholarships" awarded during his university course—not as the result of special examinations set for the purpose but based on the results of the ordinary examinations of the medical curriculum. For example, if the boy attained a sufficiently high standard in the First M.B. examination the repayment of that part of the loan pertaining to the period concerned with the course of work for this examination should be cancelled. Similar procedures should be adopted in the case of the subsequent examinations. These "post-entry scholarships" would be a strong incentive to the boy to pursue his studies diligently. The sons of well-to-do parents, of course, even though they may pay for their university education, should be subjected to the same careful selection (and elimination). The award in the *entrance* scholarship should also take the form of cancellation of repayment of a part of the loan. I am of the opinion that by such means as these a considerable improvement in the quality of the general run of medical students could be achieved.

We may observe in this place that students entering the university with a view to becoming school-teachers may receive a grant (not, if certain stipulations are fulfilled, a repayable loan) from the Board of Education to cover expenses incidental to a four-year course of study. The amount of the grant depends on the financial status of the parents and may, if necessary, cover completely all tuition and living expenses. The student is recommended to receive such a grant after interview by a selection committee consisting of members of the academic staff of the university. The only stipulation made by the Board of Education in drawing up the agreement with the student is that he promises to teach in an approved school at the end of his course. If the student after qualifying fails to comply with this obligation and does not furnish "valid reasons" for doing so, he is expected to refund the amount of the grant. A modified form of such a procedure as outlined above should not be unacceptable if it be conceded that a medically qualified person does not play a part of less importance in the State than the school-teacher.

The Anatomical Course

Then, with regard to the adverse influence which the present examination system exerts upon the education of the student, I would illustrate my suggestions by particular reference to my own subject (anatomy), the teaching of which has been the object of so much discussion recently, although like considerations can be recommended in other subjects. It will be generally agreed that the student should possess a sound knowledge of the two basic subjects, anatomy and physiology, before he is required to spend a considerable proportion of his time in clinical study. This does not imply a sharp division between the study of these two subjects and clinical studies, but it does demand that a good working knowledge and understanding of the normal structure and function of the human body should be acquired before the bulk of the student's time is devoted to the investigation of abnormal (sick) human beings. The study of "applied anatomy" and "clinical physiology" should of course be continued throughout the clinical years, and much of these matters should be dealt with by the teaching clinicians in association with the appropriate clinical cases. With regard to anatomy, I believe that the biggest bugbear with which the student has to contend is the present necessity for him to carry in his mind numerous facts —many of which he may have first encountered in the early days of his anatomical course—right up to the time of the professional Second M.B. examination, when he is expected to reply to questions involving the memory of the details of all parts of the body. This state of affairs may be remedied in the following way, and at the same time the "education" of the student can receive greater attention.

Suppose a student dissects an upper limb in the first eight or nine weeks of his course. During that time he should be tested for a *reasonably* detailed knowledge of the structure and "functional anatomy" of that limb, and he should be given to understand that he need not utilize his time in repeated endeavours to memorize those details with a view to carrying them in his mind over a period leading up to a Second M.B. examination at the end of five (or four) terms. It is common experience among teachers of anatomy that a student may "know" individual parts of the body at the time of dissection but cannot carry them in his memory for a prolonged period. The time thus saved from repeated attempts at revision of formerly dissected details is rendered available for the study of those aspects of the subject (e.g., general principles, embryology in its broadest sense, normal radiology, etc.) which enable the student to understand the significance of the structures he is dissecting. I firmly believe it is desirable that a student should become acquainted at least once with the details of the general structure of the body. Even if with the lapse of time he is forgetful or hazy concerning many of the details, he has at the back of his mind the knowledge that such structures exist and can be looked up should the occasion arise. If he does not make this acquaintance he does not know that such-and-such structures even exist, and is thus not aware of his own ignorance. Alongside this consideration it must be borne in mind that the recent developments in anatomical teaching do not form merely factual additions to the student's curriculum but are intended to render easier his understanding of the subject, and they have replaced much that was formerly given prominent attention by teachers of anatomy—e.g., the exact attachments and individual actions of muscles, exact markings on bones, exact attachments of ligaments, detailed unimportant relations of various structures, etc. Alteration of the anatomical course should not merely involve a cutting out of such-and-such structures from the syllabus. Indeed, it would be interesting (and amusing) to ask, say, 50 clinicians, medical and surgical, separately to draw up a list of the structures of the human body which could be omitted from the anatomical course. I am inclined to think that acceptance of the sum-total of their suggestions would necessitate professional anatomists looking for occupation in other walks of life. Conversely, if 50 clinicians were separately asked to draw up a list of what each considered the student of anatomy should be taught, the resultant textbook based on their suggestions would probably far exceed in bulk the ones now commonly employed.

I believe, then, that much of the present difficulty, so far as anatomy is concerned, can be circumvented by examining students at the end of each term of their course on the work done during that term, and abolishing the second professional examination. In this way we could get rid of *the premium at present placed on mere feats of memory*. So far as practical politics are concerned, this would necessitate three visits of the external examiner each year, a practice which is general even under existing arrangements. It is common knowledge among anatomists who have had extensive examining experience in a number of universities that the internal examiner (the local professor of anatomy) keeps record cards on which are entered the details of each student's terminal examination results over a period of four terms. These records are rightly consulted by all the examiners concerned in conducting the professional Second M.B. examination, and I am convinced that such detailed records render the professional examination redundant as a means of assessing whether the student should be allowed to proceed with the next part of his course. I would strongly advocate a retention of the necessity for the student to become acquainted with the general structure and function of the body, and deprecate a ruthless cutting down of the detail to be noted, though not necessarily memorized for long periods. The proper understanding of principles and the illustration of practical applications cannot be at all satisfactory in the absence of an adequate background.

While the above details refer to the subject of anatomy, similar principles might be adapted to other subjects in the

medical curriculum, the aim being to reduce the necessity for the performance of feats of memory while not ruthlessly eliminating much essential detail. With regard to pre-clinical and clinical teaching, the pre-clinical teachers (with few exceptions) are full-time teachers who have been appointed to their posts in virtue of their teaching and research experience. For the most part they are capable, thoughtful, progressive teachers, and erect the foundation on which later clinical studies are built. Compared with pre-clinical work, clinical study has more "glamour" in the student's mind, and, in general, students are more eager to learn about clinical than about pre-clinical matters. In spite of this the great majority of clinical teachers are honorary members of the staffs of teaching hospitals, the bulk of whose time and thoughts must of necessity be given to matters other than the instruction of medical students. It is becoming generally appreciated that the present status of clinical teaching would be materially improved by the appointment of an adequate staff of full-time clinical teachers. As in the case of pre-clinical teachers, the best clinical teachers are most likely to be those with research interests, eager to further knowledge and progressive in their teaching methods. It is undoubtedly true that pre-clinical studies are best approached in a scientific manner, while a considerable amount of clinical teaching must, from the nature of the work, be of the type of vocational instruction, though as time progresses and research thrives, more and more clinical study will be capable of scientific approach.

Conclusion

In effect, then, the present communication is an earnest appeal to those who are setting out to modify the medical curriculum to take into account the postulate made here, that a proper choice of student, the abolition of financial obstacles to entry into the medical profession by means of an extensive system of State aid, coupled with a ruthless weeding out of unsatisfactory students early in the course, the appointment of an adequate number of full-time clinical teachers, and modification of the existing examination system, will allow of the formulation of a high-standard curriculum. It will be strongly deprecated by many if the main alterations comprise a hasty general "simplification" of the various subjects, resulting in the degrading of the standard of work to the level of an unsatisfactory person wishing to qualify as a doctor.

Since these matters are prominent in the minds of many at the present time, the main object of this communication is to invite and stimulate comment and criticism on the *principles* here set forth, which of course represent only a few of the numerous questions which must receive consideration.

BIRMINGHAM ACCIDENT HOSPITAL

The second annual report of the Birmingham Accident Hospital and Rehabilitation Centre (which took over the Queen's Hospital building) shows that during the twelve months just upon 20,000 new patients suffering from injuries as a result of accident were treated. There were 91,000 casualty attendances, 2,174 in-patients were admitted, and 8,123 operations, many of them, of course, of a minor character, were performed. The high incidence of accidents in industry was the reason for the decision to establish this special hospital, notwithstanding the difficulties of wartime. These difficulties still remain. The old casualty and out-patient departments of the Queen's were inadequate, and plans were made for their alteration and adaptation at a cost of £20,000, but only slow progress has been made owing to shortage of labour and material. The reconstituted block will provide a reception department containing a separate shock room, three operating theatres, and *x*-ray units, and the out-patient treatment department will include a fracture out-patient suite and soft-tissue dressing and redressing stations. One matter of great concern to the board has been the difficulty of obtaining surgical staff. On the other hand, Birmingham industry has responded well both in money and good will. The hospital has become the centre for industrial medical officers and nurses and will eventually become the centre for industrial first-aid workers. The value of having a bacteriological research unit of the Medical Research Council under Prof. A. A. Miles is obvious, when it is considered that at least 11% of reportable accidents in factories are labelled septic. It is likely that the incidence is much higher than this in a large industrial centre like Birmingham, which contains a great number of small factories without either a nurse or a doctor.

Correspondence

War Neuroses, Morale, and Social Psychology

SIR,—Dr. Ronald Fairbairn's article on the war neuroses (Feb. 13) is to be welcomed as one of the most important contributions recently published on this subject. It is a typical example of the application of the Freudian method, which by bold deductions based on an imaginative understanding of the data sheds a new and brilliant light on the subject, transforming not only our understanding of the problem but also our methods of treatment. Others have recognized the existence of separation-anxiety,[1] and even possibly the dependence of the neurotic, but I have not heretofore seen this characteristic symptom welded into its place in a general theory.

My own experience as a Service M.O., having increasingly impressed me with the infantile dependence of the neurotic, has led me to conclusions similar to those of Dr. Fairbairn. Thus I have emphasized the low morale of the neurotic, as well as his desire to return home. This is recognized by the Forces in their policy of boarding out these patients. The logical (or is it illogical?) extension of this policy is seen in the suggestion that malingerers are neurotic and that even they should be boarded out.[1] That is why I venture to criticize Dr. Fairbairn's thesis, not in its essential feature but for its conclusions. For what do these conclusions come to in the last analysis? To this: that good morale counteracts the tendency to war neurosis produced by infantile dependence; but this infantile dependence itself is the very cause of the weakness of those bonds which constitute good morale. We are thus wandering in a circle, as Dr. Fairbairn recognizes when he jokingly remarks that evangelists not psychotherapists should be in charge of treatment. But what is this circle into which we have been led? The Freudian circle is the family circle.

Emotional development is a development from a state of complete dependence to independence, from no responsibility to responsibility, from absence of freedom to freedom. Freedom is pleasurable, responsibility is painful. The cost of freedom is responsibility—i.e., lack of freedom in relation to other members of the community. But man is a social animal; his sense of freedom and of independence is part of his feeling of one-ness (of identification) with the community. It is not freedom from, but freedom within, the community. In other words, the growth of freedom and of independence takes place by changing the dependence on the family for dependence on the community. But the community in its turn must be dependable: individual freedom depends on the social division of responsibility. The individual can only act responsibly in his own sphere provided the community acts responsibly, or reliably, in the rest. But how reliable is the community? How does it first strike on the developing individual? Its first impact is through the school, and from the present point of view the elementary school is woefully inadequate. (How many of us would consider an elementary school education sufficient for our own children? Yet that is all that about 90% of the population get.) And after school the individual is thrown into an environment in which mass unemployment is prevalent, malnutrition is rife, and ever-increasing insecurity the lot of all. It is not surprising therefore that emotional development from the family to the community is prevented. The stimulus is lacking. Such a development is replaced by a concept in which the community is regarded as a sort of larger family. But the family is only a constituent part of the community, in the same way that a cell is part of the body, and therefore such an attitude is regressive—i.e., neurotic.

The solution is now clear. To increase morale, to treat and prevent war neurosis, we must replace dependence on the family by the feeling of one-ness with the community, by a system of education which gives understanding of the nature and aims of the community and the part the individual has to play in it. Lest this seem mere idealistic talk, I would emphasize that such education is being used as a practical and successful method of treatment of the neuroses in the Services.[2]

[1] Good, Rankine (1942). *British Medical Journal*, **2**, 359.
[2] Jones, Maxwell (1942). Ibid., p. 276.

For obvious reasons I have compressed my opinions to the minimum space possible. The prevention of war neuroses is of the utmost importance because of its intimate connexion with morale. I hope the matter will receive the widest possible discussion, so that we may be prepared for the problems we shall meet as the war deepens in intensity and widens in range.—I am, etc.,

M. HAMILTON,
Fl. Lieut.

Planning for Treatment of Head Injuries

SIR,—May I endorse Dr. Rowland Hill's lucid and well-balanced letter (April 10, p. 457). Those of us who see many cases of head injury in which the patients have returned to civilian employment cannot fail to be struck with the persistence of symptoms, of which headache is only one. These men have, in many instances, no previous history of neurotic disability and there is evidence of previous good personality. The commonly found euphoria in these cases is also a factor which may cloud the issue and affect the diagnosis as made in hospital. On balance the recently published papers appear to be over-optimistic.—I am, etc.,

Rochampton, S.W.15. HAROLD PARSONS.

Strategy and Tactics in Research

SIR,—Dr. F. M. R. Walshe is to be congratulated on his article (April 17, p. 467). Our existing research machinery has done a great deal of good work, but there is still far too much waste and misdirection of energy.

Of recent years research has tended to become more and more a matter of work in laboratories and research institutes. Admittedly, there are some types of work which require full-time specialization, but the over-professionalization of research must inevitably admit the type of worker whose work matters less to him than his career, a danger of which Dr. Walshe's warning is timely. The final outcome of certain tendencies which are at present observable might easily be the divorce of research from practical field-work, and in future planning greater attention must be paid to the amateur in research.

The good research worker is a man who retains the logical, persistent, and often naïve curiosity of childhood. He is likely to be found in any sphere of life. Meeting in his daily round of private practice, public medicine, or hospital duties something which arouses his curiosity, he is impelled to ask "why" or "how" and to follow up his question by research. What he needs, and at present lacks, is some means of finding what work, if any, has been done on that particular problem, whether anyone else is at present working on it, what information bearing upon it, either directly or indirectly, is available, and, where necessary, laboratory and statistical assistance in the more technical details of the work. To-day his resources in respect of the first of these depend upon whether he has access to a large library and the time to use it, and the others upon his good or ill fortune in having the right individuals among his acquaintances. At present he may waste months or years on work which has already been done by someone else, or may be compelled to abandon valuable investigations for the lack of some small but valuable item of information which might be available if only he had the means of finding it.

What we need is some central organization to which any worker could apply when he felt impelled to investigate some problem. This organization could advise him as to whether investigation seemed likely to be worth while, put him into touch with other workers on kindred problems, suggest a technique of research, and provide specialized technical assistance if necessary. What it could not do is to provide him with leisure: is it beyond all our wit to devise a means by which a doctor outside the laboratory could be relieved of some part of his routine work to pursue a promising line of investigation? Cannot we also insist that a proportion of our full-time research workers shall be recruited from men and women who have spent some time in private general or special practice, or in public health or industrial work, not merely in a conscious and deliberate attempt to gain a little "experience," but in the honest work of that branch of medicine without ulterior motive? Not a few men find and develop in themselves, while engaged in clinical or administrative medicine, outstanding research ability, yet for obvious reasons cannot in middle life, under our present system, give up what they have and start a research career at the bottom of the ladder.

As Dr. Walshe points out, papers are written and published for a variety of reasons, though the spate of publication is probably less in this country than in some others. Too many still appear because a young man knows that this is the only way in which he can bring his name before the profession, and it is hard to be free from a haunting fear that man may be degraded to the status of an interesting experimental animal which is bred so that aspiring researchers shall have material. In my private Utopia men will be selected for appointment to research posts only after consideration of the papers which they have *not* submitted for publication; only the man who can set high standards for himself and reject the results of hard work because they fall below these standards can be really trusted with that dangerous drug, success.—I am, etc.,

Accrington. JOHN D. KERSHAW,
Medical Officer of Health.

The Calcium Intake in Pregnancy

SIR,—In an account of the meeting of the Scottish Group of the Nutrition Society held at Edinburgh in December, 1942, Dr. H. M. Sinclair is reported to have stated (*Journal*, 1943, **1**, 51) that in pregnancy "supplementary feeding of calcium must not be indulged in lightly since it might prolong pregnancy and harden the foetal skull." I have been unable to trace any work that supports the belief that a high intake of calcium prolongs either pregnancy (the duration of which is not easy to assess) or labour by hardening of the foetal skull. It is in fact desirable that the intake of calcium by the pregnant woman should be high, particularly during the last three months of pregnancy, when two-thirds of the foetal calcium is deposited. There is agreement among reliable authorities (Coons, C. M., *Bull. Okla. agric. exp. Sta.*, 1935, No. 223; Toverud, R. V., and Toverud, G., *Acta paediatr.*, Stockh., 1931, **12**, Suppl. 2; *Bull. Hlth. Org. L. o. N.*, 1938, **7**, 460) that the calcium requirement of the pregnant woman is 1.5 to 2 g. per day, or approximately twice the normal requirement.

Recently at this hospital certain aspects of pregnancy in primiparous women have been studied. The investigation included, among others, observations on two groups of cases, one of which ingested 1 g. and the other approximately 3 g. of calcium daily throughout pregnancy, commencing at the second month. The duration of pregnancy (so far as it is possible to measure this) and labour (first, second, and third stages) was essentially the same in both groups. In the abstract of Dr. H. M. Sinclair's paper the daily dosage of calcium which, it is suggested, might lead to a prolongation of pregnancy and labour (hardening of the foetal skull) was not given. In my preliminary observations cited above the calcium intake in one group was as high as 3 g. daily, a figure not commonly exceeded, and this dosage in no way adversely influenced pregnancy or labour. In pregnancy it would seem wiser to stress the well-established complications resulting from calcium deprivation, rather than the unproven dangers of calcium overdosage.—I am, etc.,

Middlesex Hospital. J. DOUGLAS ROBERTSON.

Asthma in Childhood

SIR,—From the articles in the *Journal* of April 3 by Sir Arthur Hurst and Dr. C. H. Rogerson one obtains the impression that both writers have been concerned with established cases of asthma.

The general practitioner has the opportunity of observing children about the age of 3 or 5 suffering from the first, or one of the first, attacks of asthma. At such an early age psychological factors are not of the same importance as in the older child, and the family doctor may obtain the help of the parents, rather than the reverse, in treating the case. The parents can be instructed never to show the slightest sign of alarm should the child have another attack and never to talk of the "wheezy noises" or let the child think there is anything unusual about the breathlessness. Should another attack appear the parents are advised not to send for the doctor, or, if they feel a visit is necessary, not to let the child know the doctor is coming. The child should be spared from sharing in the

anxious state of expectancy occasioned by waiting for the doctor.

For some years it has been my habit to examine for acetone in the urine of every child I see suffering from asthma. I was led to do this owing to the extraordinary variety of symptoms shown by children suffering from ketosis. In children under the age of 6 with asthma I have seldom been disappointed, the urine turning a deep purple colour with the sodium nitroprusside test. The most convenient way of carrying out this test is by the method described by Lawrence in his *Diabetic Life*.

Recently during the routine school examination of a boy of 10 I inquired about the attacks of asthma he had had before school age. I saw the boy in his first attack but did not diagnose asthma until he had a second. The urine showed acetone ++. He was given 1/2 teaspoonful of sod. bicarb. three-hourly in glucose and flavoured glucose drinks. The mother stated that the boy had been free from asthma for five years and that she had improved on my simple remedy by giving the child "citralka" whenever he showed the slightest sign of asthma, and the attack was aborted.

A girl from London aged 4 years was on the waiting list of a London hospital and according to the mother was to be admitted in order that skin tests could be carried out. She had a sharp attack of asthma while on holiday in Edinburgh. The urine contained acetone ++. Ephedrine 1/2 gr. and a teaspoonful of "alkagen" granules repeated in two hours, along with glucose drinks, relieved the attack, and after several doses of the alkali the child was free from symptoms. The mother reported from London three months later that the child had been free from asthma except for two threatened attacks which were banished by giving the granules and glucose without ephedrine.

Six similar cases could be quoted; most of them are in youngsters I see from time to time while visiting their homes, and not one has become an asthmatic. In my experience attacks of asthma or acidosis in children under the age of 6 result from dietetic errors or excitement. The common custom of giving young children the "top of the milk," the mother's ration of butter in addition to the child's, along with liberal amounts of cod-liver oil can readily upset the G-FA ratio. In other cases no dietetic error can be found, but the history of a period of excitement, such as a children's party or a boisterous game, may be obtained, and this may have made a heavy demand on the glycogen reserve.

I have not had the same success with children over the age of 8, as usually the attacks of asthma are well established and have become a habit, also the mother-child anxiety link has been firmly joined. There may be ketosis, but curing it does not always banish the asthma. Ultra-violet rays, breathing exercises under the supervision of a competent masseuse, vitamins, and the intelligent co-operation of the parents will do much for the child in danger of becoming an asthmatic.

The late Prof. Gulland used to say the treatment of haematemesis was to give morphia—to the relatives. He might well have included asthma.—I am, etc.,

ALISTAIR G. CRUIKSHANK, F.R.C.P.Ed.,
Temporary Assistant Physician, Royal Infirmary, Edinburgh.

Sulphonamides in Asthma

SIR,—I read with great interest the brilliant survey of the problem of asthma which appeared in your issue of April 3 (p. 403), and I venture to suggest a further hopeful line of treatment which I have been investigating. Sir Arthur Hurst mentioned the importance of bacterial infection of the nasal and bronchial mucous membranes as the primary aetiological factor in some asthmatics. He gives two reasonable suggestions of how such infections may act, to which one may add a third. Is it not possible that the bacteria themselves are the provocative allergen, as indicated by the occasional asthmatic reaction in such patients when given an excessive dose of an autogenous vaccine? No matter which is the more likely interpretation, it appears reasonable to suppose that an intermittent intensive course of one of the sulphonamides would benefit asthmatics who have any chronic, or acute recurring, respiratory infection.

During the last four months I have tried this hypothesis on such cases with apparent success. However, the number of cases, the period of observation, the lack of sufficient controls, and the use of other forms of treatment being sometimes continued by the patients themselves, do not allow me to express any definite opinion at present. I mention it partly to point out a real difference between the aetiology of the average case of asthma as seen in the British Isles and that in North America. Certainly in Canada the incidence of asthmatics with positive skin reactions to various common allergens, and with a history of hypersensitivity to corresponding foods, clothes, or dust, is very high compared with Ireland, where bronchial or nasal infection seems much more common as an exciting cause, and skin tests are often completely negative.

There seems, therefore, good reason in this climate to stress the value of the sulphonamides in asthma, in both prophylaxis and therapy, rather than the use of vaccines. In one patient, a middle-aged man referred for persistent dyspnoea consequent on chronic bronchitis and asthma, the first complete symptomatic relief after three months of constant wheezing was obtained by five days' treatment with sulphathiazole. The vital capacity increased from 1,300 to 2,400 c.cm. in approximately the same period. He had previously tried most of the usual nostrums, including vaccines.—I am, etc.,

Dublin. D. K. O'DONOVAN.

Treatment of Vomiting after Sulphapyridine

SIR,—With reference to Acting Squad. Ldr. R. O. Gillhespy's letter (April 10, p. 459) I am very pleased to confirm the importance of alkalinity of the blood and alkaline excipients in the administration of sulphapyridine. It also materially assists the alkalization process if the liver and bowel are thoroughly prepared with an adequate dose of calomel. This has been my practice in the treatment of almost 300 cases of cerebrospinal meningococcal meningitis, etc., admitted from military and civilian sources during the last seven years.

The almost startling, miraculous improvements in toxic cases of morbilli recently treated in our infectious diseases hospital by this routine have borne out the importance of alkalization in treatment with sulphapyridine. The administration of bicarbonate of soda is pushed until the urine becomes alkaline. The usual symptoms—vomiting, cyanosis, and depression—are reduced to a minimum.—I am, etc.,

G. A. DAWSON,
M.O.H., Darlington.

Blood *p*H and Haemolysis in Blackwater Fever

SIR,—I am indebted to Dr. J. F. Loutit (March 20, p. 360) and Major J. V. Dacie and Col. F. Murgatroyd (April 10, p. 458) for the information contained in their letters on the subject of the recent paper by R. Winstone Evans and me on blood *p*H and haemolysis and its application to the treatment of blackwater fever. I have corresponded privately with Dr. Loutit, but certain of the criticisms raised in the second letter seem to call for an answer, and I hope the following may clarify our position on the clinical side of the question.

The writers object to the assumption that alkalaemia was responsible for the cessation of haemolysis in our cases. We had, however, three facts before us which were independent observations. (1) The marked variations in fragility in any twenty-four-hour period in normal subjects. We could find no factor causing this, but physiological variations in CO_2 content are known to occur, and we suggested these as a possible explanation of the phenomenon. (2) A connexion between *p*H and degree of fragility of red cells was demonstrable *in vitro*. We were not aware that this had been carefully worked out before, as the full literature on the subject was not available to us at the time. (3) A case of blackwater fever had occurred in which tetany, due to ordinary treatment by alkalis, was followed by dramatic clinical improvement and cessation of haemolysis. It seems to me that, knowing this much, it would have been neglectful not to have tried the effect of inducing alkalaemia in suitable cases; and, as stated, our results convinced us subsequently of the therapeutic value of the method. Blackwater fever is sufficiently uncommon and sufficiently dangerous to justify the publication of any reasonable system of treatment if the authors are convinced of its value. Such a system should gain in value if it can be shown to be not purely empirical, and if a theory based on physiological and physical principles and experiments can be adduced to support it. This is what we have attempted to do.

In stating that a combination of jaundice and albuminuria in malignant malaria is an indication for stopping quinine we had particularly in mind cases in which repeated attacks of malaria had occurred within a short period, and in which

blackwater fever was, therefore, a likelier complication. The statement was, of course, not intended to mean that treatment should be suspended. We are only too well aware that patients may die of malignant malaria if left untreated, and a special note on the subject of using even quinine courageously is made in discussing a fatal case in the paragraph headed "Factors D and E." Our ordinary practice was to substitute mepacrine for quinine, in cautious doses, in cases where there was any reason to think that blackwater fever might supervene.

Finally, we state only that in our admittedly limited experience we did not find the pre-blackwater state as described in the textbooks. What we did find was a combination of circumstances and symptoms which made us very much on the alert for the appearance of blackwater fever, and these we have described in the article.—I am, etc.,

FELIX SMITH.

Surgical Emphysema

SIR,—The case described by Dr. Roger Stanley (April 17, p. 477) reminds me of two cases seen by me many years ago when I was a resident at Leicester Royal Infirmary.

A woman who had been knocked about by her husband sustained a fracture of the nasal bones. Whenever she blew her nose in order to get rid of blood, etc., air was blown into the subcutaneous tissues of one side of the face. Gradually the surgical emphysema spread all over the face and neck and thorax. The nose was syringed clear of blood and the patient was advised to refrain from blowing her nose. In a day or two the swelling began to disappear.

A few days later a patient was sent into the infirmary with a widespread surgical emphysema which had come on during labour. Inquiry elicited the fact that the swelling had first appeared on one side of the face. I came to the conclusion that in each case a rent had occurred in the lining probably of the lacrimal duct, and that with every expulsive effort air had been forced from the nostril into the subcutaneous tissues.

Since then, whenever I have come across a case of surgical emphysema I have inquired where the swelling first appeared. In a majority of cases this has not been accurately noticed. But the swelling has begun on "one side of the face" in a number sufficient to convince me that there is no need to presume that a chest lesion is the cause of this condition.—I am, etc.,

Bradford. JAMES PHILLIPS.

Interstitial Emphysema during Labour

SIR,—I have read with great interest the case of interstitial emphysema during labour reported by Dr. Roger Stanley (April 17, p. 477). I attended a rather similar case several years ago.

The patient was a primipara aged 18. She was somewhat anaemic but was otherwise normal. There was nothing exceptional in the medical history. Labour started on a Sunday afternoon and the baby was born at 3 p.m. on the Monday. When the head was distending the vulva the pains became more severe, and light chloroform anaesthesia was induced, and while doing this I noticed that the patient's face was becoming swollen and puffy and giving a sensation of fine crackling crepitus when the hand was passed over it. After expulsion of the placenta there was great swelling of the face and neck as well as of the chest. There was nothing abnormal during the puerperium, and at the end of twelve days all the swelling had disappeared.—I am, etc.,

Dingwall. J. J. SINCLAIR.

Diagnostic Test for Kala-azar

SIR,—On coming to this Province as Inspector-General of Civil Hospitals after many years in a specialist appointment elsewhere, I find that the "aldehyde test" for kala-azar originally discovered by me and first described in my note published in the *British Medical Journal*, 1921, **2**, 266, is now everywhere associated not with my name but with another's. The facts are that on finding this remarkable reaction in a small series of cases and realizing its immense usefulness in the diagnosis of an extremely prevalent and disabling disease (easily cured once the diagnosis is made), I wrote describing it not only to you but also to the Calcutta School of Tropical Medicine, where it was abundantly confirmed and allowed to be labelled with another worker's name.

While not disputing the value of subsequent work purely confirmatory in character, I consider I am at least entitled to share the honours. The test is extremely simple and reliable, and is, in fact, performed many thousands of times annually in North-Eastern India in a form not differing in any way from that described by me.

I may perhaps further quote from Major-General Sir Ernest Bradfield's *Indian Medical Review* (p. 206): "In 1921 Spackman introduced for kala-azar a modification of the formol-gel test of Gate and Papacostas, first used for syphilis. The test was further popularized by Napier."—I am, etc.,

Bihar, India. W. C. SPACKMAN, Col., I.M.S.

Irritant Spectacle Frames

SIR,—Dr. H. Thistlethwaite (April 17, p. 493) is apparently the first to record in this country the occurrence of sensitization following the wearing of spectacle frames of artificial tortoise-shell. In 1942 I mentioned in a letter to you (Jan. 3, p. 24) that H. S. Berkoff (*Arch. Derm. Syph.*, 1938, **38**, 746) reported a sensitization dermatitis related to the wearing for ten days of spectacle frames of synthetic resin. Berkoff believed that the tricresylphosphate used as plasticizer (non-volatile solvent) in the resin was the irritant agent. It is surely important to ascertain if tricresylphosphate had been used in the present material, and, if so, to test Dr. Thistlethwaite's patients for dermal sensitivity to this substance. Confirmation of Berkoff's results would be an obvious indication for action on the part of the profession in its modern role as guardian of the common man against the products of the synthetic chemist, especially in view of the wide use of artificial resins from babies' toys to suspender clips.—I am, etc.,

Department of Pathology, the University, Glasgow. A. C. LENDRUM.

SIR,—Dr. H. Thistlethwaite (April 17, p. 493) has observed a new form of allergy. Being myself susceptible to this form I noticed that for at least three weeks after buying new spectacles the condition was acute. I at first thought the irritation was due to close-fitting sides or a tight bridge, but it soon became evident that the composition of the frames was to blame, though what precise chemical I am unable to state. There were in the past three years at least ten other cases, but not all the patients bought their spectacles from the same retailer, though I believe that all the frames in this part of the country are supplied by the same manufacturer and are now of the same shape and material.

Treatment in those cases where the spectacles are worn all day consisted in covering the frames—the sides and bridge—with fine darning silk, when the condition improved rapidly. In other cases a 10% solution of ichthammol on lint at night-time proved very effective.—I am, etc.,

J. E. KING.

The Services

Temp. Surg. Lieut. J. K. Thomson, R.N.V.R., has been appointed M.B.E. (Military Division) for skill and devotion in tending wounded survivors from a torpedoed merchantman, and Temp. Surg. Lieut. G. J. Laws, R.N.V.R., has been mentioned in dispatches for good services during operations off North Africa.

CASUALTIES IN THE MEDICAL SERVICES

Capt. GEORGE MACBETH CALDER, R.A.M.C., who was wounded in action in the Middle East in Oct., 1942, died from the effects of his wounds last month. He was the eldest son of Prof. W. M. Calder, LL.D., of Edinburgh, and graduated M.B., Ch.B. at Edinburgh University in 1936. After holding hospital appointments in England and Scotland he was specializing in psychiatry under Prof. D. K. Henderson when war broke out.

Flying Officer HAROLD PATTERSON HALL, R.A.F.V.R., who was killed in a flying accident on March 12, was born in Oct., 1914, and studied medicine at Newcastle-upon-Tyne, taking the Scottish triple qualification in 1941. After holding a house appointment at a mental hospital he received a commission in the medical branch of the R.A.F. on April 3, 1942, and at the time of his death he was M.O. to a fighter squadron.

Wounded.—Capt. G. O. Brooks, G.M., R.A.M.C., Lieut. H. B. Cowan, R.A.M.C., Temp. Col. J. H. Donnelly, R.A.M.C., Major L. H. G. Moore, R.A.M.C.

Obituary

The death occurred on March 15 at Binbrooke, after a long and trying illness, of Dr. WILLIAM J. WILKINSON, a well-known practitioner in North Lincolnshire. He was 65 years of age, and was born and brought up in Lincoln, where his father practised in partnership with the late Dr. Brooke. His mother was a sister of the late Mr. W. H. Battle, the well-known St. Thomas's Hospital surgeon. He did his medical training at St. Thomas's and qualified in 1905. Over thirty years ago Dr. Wilkinson started to practise at Binbrooke, and was M.O.H. to the Louth Rural District Council from 1919 until he retired from the appointment last year. He had been a member of the B.M.A. since 1911, and was chairman of the Lincolnshire Division in 1933–4 and also served on the Executive Committee for some years. Dr. Wilkinson was friend as well as physician to many families, rich and poor, in the scattered country district in which he worked, and no doctor was held in higher regard in the Lincolnshire Wold area. His wife survives him; also a son, Dr. John Wilkinson, who is carrying on the Binbrooke practice.

We regret to record the death last summer at Kyrenia, Cyprus, of Dr. ARTHUR ELDON SCOTT. He studied medicine at the Middlesex Hospital, and after qualifying M.R.C.S., L.R.C.P. in 1896 was resident medical officer at the North-West London Hospital. He served in the last war and afterwards joined the Public Health Service of the Egyptian Government, becoming assistant M.O.H. for Cairo City, and receiving the 4th Class of the Order of Ismail in 1926. Dr. Eldon Scott joined the British Medical Association in 1897, and held office as president of the Cyprus Branch in 1937–8. He was a prominent Freemason.

News has been received of the death on Oct. 15 in Jersey of Mr. ARNOLD SAMUEL FERGUSON, throat, nose, and ear surgeon to the Jersey Dispensary and Infirmary, and aural and ophthalmic surgeon to the Jersey General Hospital. Mr. Ferguson qualified from the Middlesex Hospital in 1893 and obtained the F.R.C.S.Ed. in 1895 after serving as demonstrator of anatomy at the Middlesex Hospital and house-surgeon at the London Throat Hospital and the Oxford Eye Hospital. He was a member of the Anatomical Society and of the Laryngological Section of the Royal Society of Medicine, and joined the British Medical Association in 1893, holding office as chairman of the Jersey Division in 1926–7. He contributed to these columns a number of notes on practical aspects of ophthalmology.

Universities and Colleges

UNIVERSITY OF GLASGOW

A graduation ceremony was held on April 17, when the following medical degrees were conferred:

M.D.—[1]G. H. Bell, [2]W. S. W. Guthrie, [3]G. Shearer, A. McPhater.

M.B., CH.B.—J. F. Allan, R. P. R. Allan, A. Armour, Janet Y. Baird, Mary MacN. Baird, W. A. Baird, J. Berkeley, J. D. Binning, R. B. Bonar, R. P. Brittain, J. A. M. Broadfoot, H. B. Brown, R. A. P. Brown, R. J. Calvert, J. Campbell, Margaret M. Chalmers, Isobel J. Cochrane, H. W. Collins, W. Cormack, J. V. Coyle, M. C. Crawford, J. T. Cunningham, R. Dallachy, W. H. C. Donald, T. Dougray, J. MacK. Dunn, Louise E. Elbert, Elizabeth G. Fenwick, Catherine B. Foster, N. J. Fraser, D. J. Gracie, G. E. Griffiths, W. R. Hope, R. A. Houston, A. McI. Hyndman, N. Hyndman, S. E. Jackson, H. F. Jarvie, Anne-Marie Kivlichan, J. Lapraik, E. Leahy, Margaret C. Leitch, A. Lindsay, G. G. Lindsay, S. V. Livingstone, W. Lockhart, W. J. Logan, M. D. MacAffer, Hope J. B. McAlpine, D. Macdonald, J. H. McDougall, J. McFadden, A. Macfarlane, D. McGill, A. R. McGregor, J. J. McGrotty, O. A. MacKenzie, A. H. MacLean, R. D. H. Maxwell, A. W. Mearns, R. M. Mill, J. H. Mitchell, D. S. Montgomery, J. MacI. Moore, Anna F. S. Neil, Margaret B. C. Orr, Millie M. J. Peralta, Muriel H. Reid, C. D. Rigg, J. D. P. Robertson, J. R. Rowell, J. McG. Shaw, A. Smellie, H. G. Smith, A. Somerville, W. Thorburn, C. Wood, W. Wood, J. P. Young.

[1] With honours. [2] With high commendation. [3] With commendation.

The following prizes among others were awarded:

University Prizes.—Bellahouston Medal: W. F. Anderson. Capt. H. S. Ranken, V.C., Memorial Prize: A. R. Currie, G. B. S. Roberts (equal).

Special Class Prize.—Surgery, Macleod Medal: A. G. Melrose.

CONJOINT BOARD IN SCOTLAND

The following candidates, having passed the requisite examinations, have been admitted L.R.C.P.Ed., L.R.C.S.Ed., L.R.F.P.&S.Glas.:

G. W. M. Armistead, J. Carey, J. Connor, W. B. Cowper, J. E. Dawson, G. T. Donald, T. H. Forrest, B. C. Greenhill, Lore M. Hasslacher-Traub, Barbara V. Hastings, R. E. Heap, Daphne M. E. Kayton, H. Kraus, F. H. Leckie, J. McAllister, J. J. McMurray, J. J. MacPherson, R. R. Mahlangeni, D. R. Martin, J. E. Miller, H. A. Myers, D. Naidoo, Caroline N. Nompozolo, R. M. Oliver, Bridget Purcell, Y. D. Sethi, J. M. Stirling, Roza Szteinhaus, N. R. B. Turner.

O. Fehr, a graduate of a recognized foreign university, was also admitted a licentiate.

Medical Notes in Parliament

Comprehensive Health Service Plans

On April 15 Mr. SORENSEN asked Mr. Ernest Brown when his plans for a comprehensive medical and health service were likely to be brought before the House. Mr. BROWN replied that preliminary discussions were taking place with representatives of the medical profession, local authorities, and voluntary hospitals. He contemplated publishing in advance of the introduction of legislation, and, he hoped, in the course of the next two or three months, a general statement of his proposals, which would afford all concerned an opportunity of considering and criticizing them. The plan would not include the mental hospital and mental deficiency services.

Nurses Bill

The second reading of the Nurses Bill was moved in the House of Lords on April 13. This measure has already passed through the House of Commons. Lord SNELL said there was a need for competent assistant nurses who might not reach the qualification set out in the State Register but might be admirable practical nurses when under supervision. Hospitals for chronic patients largely depended on the services of these assistant nurses. Some reports on the nursing profession had proposed that it should be an offence for any person other than a State-registered person or an enrolled assistant nurse to care for the sick habitually for gain, and that had been recommended by the Nursing Reconstruction Committee over which Lord Horder presided, but Mr. Brown felt unable to accept the suggestion.

Lord HORDER said that the nursing profession would welcome the Bill along with the economic adjustments recommended by the Rushcliffe Committee. The two things together would raise the status of the nursing profession in this country. No man or woman who could not be put into the categories of State-registered nurse, assistant nurse, and student nurse should be allowed to attend the sick person. Lord RUSHCLIFFE said that in some local authority institutions 40% of the nursing staff were assistant nurses.

The Bill was read a second time.

Committee on Penicillin

Sir ANDREW DUNCAN reported on April 13 that the first meeting had been held on Oct. 13, 1942, of a committee to report on penicillin. The object of the committee was to secure that all available information regarding clinical and chemical trials and methods of production was collected and exchanged and everything possible done to promote rapid development. The committee included: Prof. A. Fleming, Prof. H. W. Florey, Prof. H. Raistrick, Sir Robert Robinson, Dr. C. R. Harington, Dr. A. N. Drury, Dr. V. D. Allison, Prof. I. M. Heilbron, and Lieut.-Col. Sir Russell Wilkinson, together with representatives of firms engaged in production of penicillin.

Diphtheria and Immunization in Germany

Mr. ERNEST BROWN stated on April 15 that there was no general immunization against diphtheria in Germany, but it appeared to be used locally in epidemics. The much-increased prevalence of the disease in Germany, and the fact that there had been no serious increase in two enemy-occupied countries where immunization was fairly complete, lent support to the British Government's policy in advocating the immunization of children in this country.

Army Education on Venereal Diseases

Answering Mr. Beaumont on April 13 Sir JAMES GRIGG said all officers in medical charge of units had been instructed to give periodical lectures to troops on the subject of venereal disease. Education was a slow process, but he was satisfied with that being made. Notice Board Information No. 28 explained the purpose of Defence Regulation 33B and the action soldiers should take as a result of it. The possibility of issuing films and literature on this subject had not been overlooked, but it was not thought that any at present available would prove effective.

Examination in Services by Women M.O.s

Mr. BELLENGER asked questions about routine examination of men in the Forces by women medical officers. On April 13 Sir JAMES GRIGG replied that soldiers who objected to a complete medical examination by a woman medical officer were not entitled to ask for a male medical officer, but if one were in fact available he would normally carry out the inspection. Women medical officers were usually posted to units or localities

where A.T.S. were largely employed. On April 14 Sir ARCHIBALD SINCLAIR said R.A.F. personnel could be compelled to undergo routine medical inspection which might be undertaken by a woman medical officer. In practice male medical officers performed these duties save in very exceptional circumstances. On the same day Mr. A. V. ALEXANDER said that in the Navy it would be very exceptional for women medical officers to examine personnel other than members of the W.R.N.S. and the nursing services. In an emergency, if a male medical officer were not available, it might be necessary for an officer or rating of the Royal Navy to undergo examination or treatment by a woman medical officer. The Navy had not a large number of women medical officers.

EPIDEMIOLOGICAL NOTES

Discussion of Table

In *England and Wales* the following infectious diseases were less in incidence than in the previous week by the figures given after each: measles 1,512, scarlet fever 220, pneumonia 204, whooping-cough 124, diphtheria 69.

The only large variations from the totals of the preceding week for diphtheria and pneumonia occurred in Lancashire, where there were respectively 37 and 44 fewer cases. Yorks West Riding recorded the largest drop for whooping-cough, 41 cases. In London and the south-eastern counties scarlet fever tended to rise, though there was a general fall elsewhere.

For the counties the figures given represent the extent of the decline in measles: Durham 284, Essex 202, Lancashire 197, Staffordshire 185, Warwickshire 177, Gloucestershire 173, Hertfordshire 165, Nottinghamshire 123, Devonshire 112, London 107. Increased incidence was recorded in several counties, the largest being Derbyshire 129, Kent 88, Norfolk 84, Surrey 72.

Notifications of dysentery went up by 7 during the week. An outbreak involving 40 persons was reported from Gloucestershire, Cheltenham M.B. Half of the remaining 76 cases were notified in three counties: Yorks West Riding 13, Lancashire 12, and London 11.

In *Scotland* measles was up by 118 cases and whooping-cough by 54, but acute primary pneumonia was down by 60 cases. The higher incidence of measles was due mainly to the epidemic in Glasgow, where notifications rose from 364 to 449. In Edinburgh the cases went up from 139 to 150. The increase in whooping-cough was due to the experience of the same two cities, which recorded increases of 19 and 32 respectively.

In *Eire* another 3 cases of typhus were notified in Co. Leitrim, Carrick-on-Shannon No. 1 R.D. This brings the total cases in this area to 19 in the past three weeks.

In *Northern Ireland* there were 317 cases of measles, compared with 99 in the preceding week: Belfast C.B. 110, and Lisnaskea R.D. 207.

Winter Epidemics

The returns of the fourth war winter now having been completed, it is of interest to compare the experience of the past winter with that of the three preceding ones. The general experience compares favourably with that of the previous war winters. The notifications for 26 weeks—the first 13 of the year and the last 13 of the preceding one—are:

	1939–40	1940–1	1941–2	1942–3
Scarlet fever	30,284	38,647	31,525	61,492
Diphtheria	21,451	31,608	24,992	22,041
Acute pneumonia	30,032	29,683	26,800	27,450
Cerebrospinal fever	5,432	6,138	3,879	2,176
Dysentery	1,130	2,902	3,671	3,378
Paratyphoid and typhoid fevers	518	637	774	359
Measles	—	370,780	36,132	343,759
Whooping-cough	—	69,403	41,974	37,283
Deaths from influenza in the 126 great towns	4,935	2,554	1,186	1,487

During the past year the incidence of scarlet fever was twice that of the previous winters, but the other infectious diseases common to childhood—diphtheria, measles, and whooping-cough—were at a lower level. The relative position of diphtheria is probably somewhat better than the actual figures suggest, because there has been an increase during the war of the proportion of diagnostic errors. The incidence of paratyphoid and typhoid fevers has been exceptionally light, but dysentery has remained at a high level.

The Week Ending April 17

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 2,058, whooping-cough 1,944, diphtheria 723, measles 16,732, pneumonia 1,139, cerebrospinal fever 103, poliomyelitis 5, dysentery 107, paratyphoid 3, typhoid 11. The deaths from influenza recorded in the 126 great towns for the week numbered 43.

No. 14

INFECTIOUS DISEASES AND VITAL STATISTICS

We print below a summary of Infectious Diseases and Vital Statistics in the British Isles during the week ended April 10.

Figures of Principal Notifiable Diseases for the week and those for the corresponding week last year, for: (a) England and Wales (London included). (b) London (administrative county). (c) Scotland. (d) Eire. (e) Northern Ireland.

Figures of Births and Deaths, and of Deaths recorded under each infectious disease, are for: (a) The 126 great towns in England and Wales (including London). (b) London (administrative county). (c) The 16 principal towns in Scotland. (d) The 13 principal towns in Eire. (e) The 10 principal towns in Northern Ireland.

A dash — denotes no cases; a blank space denotes disease not notifiable or no return available.

Disease	1943 (a)	1943 (b)	1943 (c)	1943 (d)	1943 (e)	1942 (Corresponding Week) (a)	1942 (b)	1942 (c)	1942 (d)	1942 (e)
Cerebrospinal fever	92	4	36	7	11	199	8	47	1	6
Deaths		—	—				1	3		
Diphtheria	729	49	185	89	33	736	37	210	35	17
Deaths	13	—	1	5	1	25	—	5	—	—
Dysentery	116	11	29	—	—	168	12	95	—	—
Deaths		—		—	—		1		—	—
Encephalitis lethargica, acute	1	—	—		—	5	—	1		—
Deaths		—	—				1	—		
Erysipelas		—	47	4	1		—	43	10	5
Deaths			—					—		
Infective enteritis or diarrhoea under 2 years				16					4	
Deaths	58	11	7	17	4	37	6	13	—	1
Measles	18,056	1,059	792	38	317	3,757	287	218	158	29
Deaths	21	2	4	—	1	3	—	2	1	1
Ophthalmia neonatorum	74	3	25	1	1	73	1	24	1	—
Deaths										
Paratyphoid fever	3	—	2			6	—	2		
Deaths	—	—	—		—	—	—	—		—
Pneumonia, influenzal*	1,290	90	15	10	15	1,089	54	18	4	4
Deaths (from influenza)	62	4	1	—	—	33	2	3	—	1
Pneumonia, primary			244	23				320	23	
Deaths		—		6	16		43		1	12
Polio-encephalitis, acute	2	—				—	—			
Deaths		—					—			
Poliomyelitis, acute	4	—	2	2	—	2	1	—	—	—
Deaths		—					—			
Puerperal fever		2	26	2	—		1	13	1	—
Deaths		—					—			
Puerperal pyrexia	173	7	21		1	187	13	18		—
Deaths										
Relapsing fever	—	—			—	—	—			—
Deaths										
Scarlet fever	1,993	209	268	41	58	939	45	157	56	31
Deaths	2	1	—	—	—	1	—	—	—	—
Small-pox	—	—	—		—	—	—	—		—
Deaths	—	—	—	—	—	—	—	—	—	—
Typhoid fever†	6	—	1	5	5	3	—	5	6	2
Deaths	1	1	—	1	—	—	—	1	—	—
Typhus fever	—	—	—	3	—	—	—	—	1	—
Deaths	—	—		—	—	—	—		—	—
Whooping-cough	1,954	168	268	23	18	1,269	154	43	22	11
Deaths	19	5	4	3	—	14	2	—	—	—
Deaths (0–1 year)	419	45	71	49	32	370	41	78	34	23
Infant mortality rate (per 1,000 live births)										
Deaths (excluding still-births)	4,772	634	644	241	158	4,796	680	733	248	125
Annual death rate (per 1,000 persons living)			14·5	15·8	‡			10·5	16·6	‡
Live births	6,596	782	992	440	311	5,731	589	924	336	230
Annual rate per 1,000 persons living			20·2	28·9	‡			19·1	22·4	‡
Stillbirths	236	23	39			253	24	34		
Rate per 1,000 total births (including stillborn)			38					35		

* Includes primary form for England and Wales, London (administrative county), and Northern Ireland.

† Includes paratyphoid A and B for Northern Ireland.

‡ Owing to evacuation schemes and other movements of population, birth and death rates for Northern Ireland are no longer available.

Medical News

Prof. E. D. Adrian, O.M., M.D., F.R.S., will deliver the fifth Sharpey Schafer Memorial Lecture, on "The Sensory Areas of the Brain," on Thursday, May 6, at 5 p.m., in the University New Buildings, Teviot Place, Edinburgh. All interested are invited to attend.

Dr. Karl T. Compton will deliver the Pilgrim Trust Lecture on "The Organization of American Scientists for the War" before the Royal Society, at Burlington House, W., on Thursday, May 6, at 4.30 p.m.

A sessional meeting of the Royal Sanitary Institute will be held at Harrogate on May 15, when papers will be read on "Rheumatism in Relation to Industry" by Dr. S. A. Underwood, and "Treatment Facilities for Rheumatism at Harrogate" by Dr. W. Edgecombe. Dr. R. Sutherland will speak on "Health Education."

The National Council for Maternity and Child Welfare (117, Piccadilly, W.1) has arranged a conference on the conditions of children in the occupied countries of Europe, to be held at the Royal Institution, Albemarle Street, W., on Thursday, May 6, at 2.30 p.m., with Lord Dawson in the chair.

An editorial in the April issue of *Mother and Child* (No. 1, vol. xiv) announces that this journal, founded in 1908 under the title of *National Life*, is now the official organ of the National Baby Welfare Council, with its 47 affiliated societies. The office is at 29, Gordon Square, W.C.1, and the price of each monthly copy is 1s.

Among the new Justices of the Peace for Monmouthshire are Dr. John Henry Verwey and Mr. D. N. Rocyn Jones, M.D., F.R.C.S.Ed.

A medical field service school, to train medical officers serving with United States Army units in the field, has been opened at the American school centre in England.

On April 6 at Grimsby Police Court a woman aged 23 was sentenced to three months' imprisonment, under Defence Regulation 33B, for not complying with the medical officer's notice to be treated for venereal disease. The town clerk said that there was no desire to punish this woman, but the Health Department sought aid in doing something necessary for the well-being of the public.

Letters, Notes, and Answers

All communications in regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON, W.C.1.

ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated.

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TELEPHONE No.—B.M.A. and *B.M.J.*: EUSTON 2111.

TELEGRAPHIC ADDRESSES.—EDITOR, *Aitiology Westcent, London*; SECRETARY, *Mediecra Westcent, London*.

B.M.A. SCOTTISH OFFICE: 7, Drumsheugh Gardens, Edinburgh.

ANY QUESTIONS?

Nicotinic Acid for Neuralgia

Q.—*Has the treatment of trigeminal neuralgia with nicotinic acid proved to be successful? If so, is it of any value in other forms of neuralgia and neuritis?*

A.—On the supposition that the paroxysms of trigeminal neuralgia are ischaemic in origin, the condition has been treated with vasodilator drugs, including nicotinic acid. In seven cases treated with doses of nicotinic acid ranging from 50 mg. twice daily to 75 mg. four times daily, there was improvement in each instance. But this work awaits confirmation. So far as is known, nicotinic acid has not been used in other cases of neuritis and neuralgia. In the past many forms of treatment have been reported to effect temporary improvement in trigeminal neuralgia, but most of them have subsequently fallen by the wayside. There can be no doubt that structural changes occur in the trigeminal nerve to produce such a sustained and intractable syndrome. Injections of alcohol and division of the sensory root still remain the fundamental treatment.

Gonococcal Reinfection and Stricture

Q.—*A patient aged 59 had gonorrhoea at 26. He noticed a gleety discharge in August, 1942. He also has a stricture which only allows the passage of a bougie No. 6 (English). He was treated with sulphadiazine 4 g., lasting for fourteen days on four separate occasions, and the stricture was dilated to No. 13 (English). There is now only the slightest trace of a clear discharge and no heavy threads in the urine, which is normal. Slides showed the gonococcus on the first occasion, but repeated examinations have shown no gonococcus, a very few white cells, and small numbers of Gram-positive diplococci and Gram-negative coliform bacilli. The bacteriologist thinks these are a secondary infection. Is this man infectious?*

A.—Assuming that gonococci were found in August, 1942, this appears to be a reinfection, since a relapse after 33 years is very improbable. The fact that gonococci disappeared rapidly under sulphadiazine therapy, which was more than adequate, suggests that the gonorrhoea is cured and that the patient is non-infectious. The clear discharge is probably due to the stricture and secondary infection. The anterior urethra should be examined with a urethroscope for the presence of follicles, and the prostatic and vesicular secretions by smear and culture; a gonococcal complement-fixation test would be useful. If the results of these are negative it may be assumed that the gonorrhoea is cured; nevertheless, it should be borne in mind that the sulphonamides are less effective when closed foci are present than when there is good drainage, and all tests should be repeated on several occasions. It is important that the stricture should be dilated periodically, up to 16 English; otherwise it is certain to contract.

Pain in the Fore-foot

Q.—*What treatment is recommended for a painful foot resulting from flattening of the metatarsal arch?*

A.—There are numerous causes of pain in the fore-foot. Did it come on after a cross-country run, route march, or P.T.; or insidiously for no apparent reason? Are the toes deformed and painful on movement? Is the patient subject to rheumatism, or has he had a recent infection? Has he lately been convalescent after an accident, operation, or other illness? Are there any callosities? Is the pain localized to any metatarsal head?

All these questions are pertinent. "Flattening of the metatarsal arch" is not a diagnosis. Assuming that the toes are not deformed, that the pain came on insidiously and is localized to the third or fourth metatarsal head, a well-applied pad will give relief. Don't suggest that the patient should buy a pad. They are usually not efficient, and in any case the trouble may be only temporary. A chiropodist will apply a protective pad, and probably in a week or two the pain will disappear spontaneously.

There are not many mechanical conditions of the fore-foot the pain of which cannot be greatly relieved by a good chiropodist. If one or more toes are painful on movement and tender on the dorsum as well as underneath the metatarsal head, physiotherapy, heat massage, and exercises, combined with curtailment of activities for a week or two, is the best treatment. If this is impossible the toe can be worked loose after a hot bath night and morning, and a metatarsal bar applied to the boot will give some measure of rest to the toe. If the pain in the foot synchronized with an infection of some kind, then rest and soothing physiotherapy are essential. There should be no compromise; in the long run time is saved. If it came on after an accident at P.T. or cross-country run, the pain is probably due to bruising or strain, and a protective pad well applied by a good chiropodist is all that is necessary. If the pain has resisted all other treatment a manipulation by an orthopaedic surgeon, followed by physiotherapy, will probably help.

INCOME TAX

Entertainment Expenses

"L. S." is informed that the Commissioners for the Division in which he is assessed have repeatedly ruled on appeal that entertaining expenses cannot be allowed to professional men.

*** We understand that this is a not uncommon view, notwithstanding that such expenditure would be allowed to business men when spent to attract custom. The legal position is governed by Rule 3 (*a*) applicable to Cases I and II, Schedule D, which provides that "any expenses not being money wholly and exclusively laid out or expended for the purposes of the trade or profession" shall not be deducted. On the facts as put by our correspondent this attitude imposes a hardship—i.e., in a case where custom dictates the necessity, or at least the advisability, of affording hospitality solely for reasons of professional gain. The prospects, however, of upsetting such a decision by an appeal to the High Court are not tempting, particularly because, unless the Court holds that there are no grounds on which they could have arrived at their decision, the verdict of the Commissioners on a question of fact is final.

Miscellaneous Queries

D. R.'s inquiries are answered below.

1. No allowance is due for "repayment of a loan"; it is a transaction of a capital nature.

2. A wife's earnings are taxed on the amount of her earnings less one-tenth earned income relief (unless her husband has had the maximum of £150) and less a special allowance of £80. The £165 payable at the reduced rate of tax—i.e., 6s. 6d.—applies to the joint and not to the separate incomes.

3. Whether parents "partially dependent" on a taxpayer create a claim to "dependent relative relief" depends on the circumstances. The parent must be "maintained" by the taxpayer and his (or her) own income must not exceed the statutory limit.

4. The cost of replacing textbooks is admissible in calculating liability under Schedule D, but not where Schedule E applies, as it does in the case of income from an appointment. In neither case is the cost of starting or improving a professional library permissible.

Allowance received for Travelling Expenses

"Z. Y." is a part-time anaesthetist in the E.M.S. and receives a salary of £360 per annum plus £100 per annum for travelling expenses. Is he liable on the £100?

*** No, unless the circumstances are such that the £100 includes an amount which is in effect additional remuneration.

LETTERS, NOTES, ETC.

The Oxford Ether Vaporizer

Dr. J. B. H. HOLROYD (Sheffield Royal Infirmary) writes: I fully agree with Dr. Elam's letter (Feb. 20, p. 232) on the Oxford vaporizer; I think this machine is most efficient in every way. I have been using it for several months and my findings are the same as Dr. Elam's. I find that it is very easy to handle and very easy to learn. The students who pass through my hands at the Royal Infirmary are all taught to use it, and, without exception, find no difficulty in getting really proficient. I have tried it on all manner of cases, good risks and bad ones, and get the same satisfactory results. I have never selected the cases, so that I could give the machine a severe trial. A most important finding is that, compared with open ether, a saving of about 60% of ether was obtained in my series of cases and without any complications. I fully endorse Dr. Elam's remark: "the apparatus of choice for the general practitioner anaesthetist."

Histamine for Psoriasis

Dr. E. HAYLING COLEMAN (Wolverhampton) writes: Some time ago I had an experience somewhat similar to that described by Dr. J. S. Knox (April 3, p. 426). I was treating a case of gastric ulcer with injections of larostidin—i.e., histamine—when to my surprise an old-standing psoriasis rash disappeared. I was so impressed that I looked round for another case of psoriasis to try it on. Again the result was most marked and satisfactory. Unfortunately both are now showing signs of a return of the rash and will need a further course of injections, but the remission has lasted several years.

Age and Perforated Gastric Ulcer

Mr. D. J. P. O'MEARA (Bury St. Edmunds) writes: Dr. Kyle of Brecon reports a case of perforated gastric ulcer in a soldier of 19 years (March 20, p. 370) and remarks that it is unusual at such an age. I have no statistics available, but I thought it might interest him and others to hear of a case of perforated gastric ulcer in a boy of 16 years, who was admitted into the West Suffolk Hospital under my care on June 23, 1941. He was an apprentice engineer, with a history of indigestion for 5 days before admission. Some hours before he was admitted he was seized with acute abdominal pain and vomiting. At operation a small perforated "acute" ulcer was found on the lesser curvature and was repaired. Convalescence was uneventful. Of some interest, too, is a patient of mine, now aged 62, who has had a perforated gastric ulcer on three occasions—in 1927, 1930, and 1935. I did not operate on him in 1927, when he had a gastrojejunostomy performed at the same time. On account of numerous adhesions the last gastric perforation had formed a local abscess before surgical help was requested. Since his last operation, despite a severe attack of pneumonia last year, he has been in fairly good health, with occasional attacks of "indigestion." These attacks are usually accompanied by a call for a visit in case he has "burst again."

Mr. J. R. M. WHIGHAM (St. Andrew's Hospital, E.3) writes: Dr. Kyle will be interested in the article by Lee and Wells, "Perforation *in utero* of a Gastric Ulcer" (*Ann. Surg.*, July, 1923, p. 36). Gastric and duodenal ulcers seem to occur at all ages, and rare instances of perforations in infants and children are to be found in the literature from time to time. My personal experience of cases in patients under 20 consists of two boys aged 17 and 16 respectively, who collapsed at work, with a doubtful period of three weeks' indigestion previously in the case of one of them. Both ulcers were gastric, situated near the pylorus, and at operation simple suturing (with peritoneal drainage in one instance) was successfully performed. The first boy required a gastro-enterostomy two years later (1939) for the recurrence of gastric symptoms, but he has since remained well.

Dr. E. C. EDWARDS writes: Dr. D. Kyle's case prompts me to record an almost similar case which recently came under my care. A healthy-looking young soldier of 20 was admitted to Penzance Hospital suffering from an attack of vomiting with severe abdominal pain, which had developed suddenly three hours before admission and without any previous symptoms. From the history and physical signs I had no difficulty in diagnosing a perforated gastric ulcer and at once performed laparotomy. A perforated small acute gastric ulcer with no surrounding induration was easily found on the anterior surface of the stomach one inch from the pylorus, with a fair amount of stomach contents free in the peritoneal cavity. The perforation was sutured and the patient made an uninterrupted and rapid recovery. The interest of the case seems to lie in the youth and otherwise good health of the patient without any previous symptoms of gastric discomfort.

Infection in the Crowded Surgery

Dr. J. F. PAYAN (Barkingside) writes: It must have occurred to every busy practitioner during these last few weeks how little good we are really imparting to our patients crowded in a stuffy "blacked-out" waiting-room. To see babies in arms inhaling air polluted by bacteria expectorated by the older patients fills me with apprehension. Some of these little creatures may be suffering from some teething disorder, but little do their mothers realize that, before leaving, their babies are already potential sufferers from some more evil complaint. What are we to do? Pressure of work and shortage of petrol preclude doctors from visiting many of these patients at their homes. The ignorant mother wants just advice, which she must obtain after passing through the "lethal" chamber. I wonder that some ingenious person has not devised a mask (not too hideous) for patients to wear when visiting their doctors. How much sickness and unnecessary work would then be prevented?

Training in Preventive Medicine

Dr. S. T. BEGGS (Morecambe) writes: It is contended that a different outlook on medical practice is required in the reorganization of the profession. This can only be brought about in the training of the medical student. Great stress has been placed on preventive medicine both in the Beveridge report and by the Ministry of Health. The student can be directed to this side of medicine only by making the qualification in preventive medicine equal to that in medicine and surgery, so that in a university final the degrees would be bachelor of medicine, bachelor of surgery, bachelor of public health. This should not add greatly to the curriculum except that a six-months attendance would be required at all departments in the public health service of a county borough.

Treatment of Scabies

Dr. R. T. BRAIN writes in reply to Dr. Spackman's letter in the *Journal* of April 17 (p. 496): I was impressed by Dr. Graham's article on scabies treated with one application of benzyl benzoate, which adds support to Mellanby's view that disinfection of the fomites is unnecessary, and it appears to be uneconomic for the local authorities to continue the mass disinfection of patients' clothing. On grounds of hygiene alone I would still advise the thorough washing of sheets and underclothing, as mentioned in my article in the April number of the *Practitioner*, and, moreover, it does eliminate one of the factors, admittedly the least important, accounting for reinfection. I also maintain that although the efficacy of a single treatment given by trained personnel has been demonstrated it would be unwise to depend upon an equivalent standard of efficiency in the home.

Textbooks for Medical Students in Malta

Mr. DAVID PYKE, on behalf of the British Medical Students' Association (B.M.A. House, Tavistock Square, W.C.1), writes: May I appeal to any of your readers who possess unwanted medical textbooks? We have received a letter from the Students' Representative Council of the University of Malta saying that they are desperately short of essential books, mentioning: *Gray's Anatomy, Bigger's Bacteriology, Cushny's Pharmacology, Clark's Applied Pharmacology, Price's Medicine* or *Osler's Medicine, Green's Pathology*, and *Kerr's Obstetrics*. Most of the students at present have no books; the lucky ones have them dating from Lister's time. I believe that before the war students from Malta completed their training abroad, and that the opening of a clinical teaching department, combined with great shortage of shipping space, has produced the present difficult situation. We have been assured of every possible help by the Colonial Office, and therefore anyone who is kind enough to send medical textbooks to us may feel certain that every endeavour will be made to see that they reach our brave friends in Malta.